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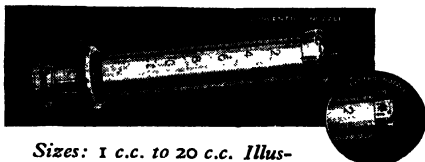
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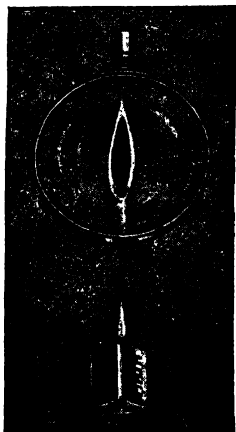


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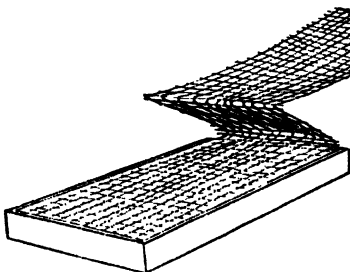
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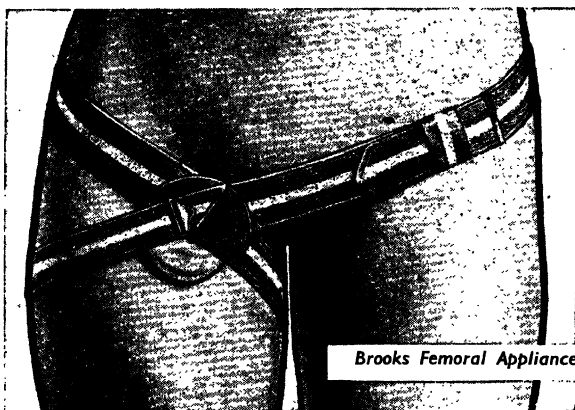
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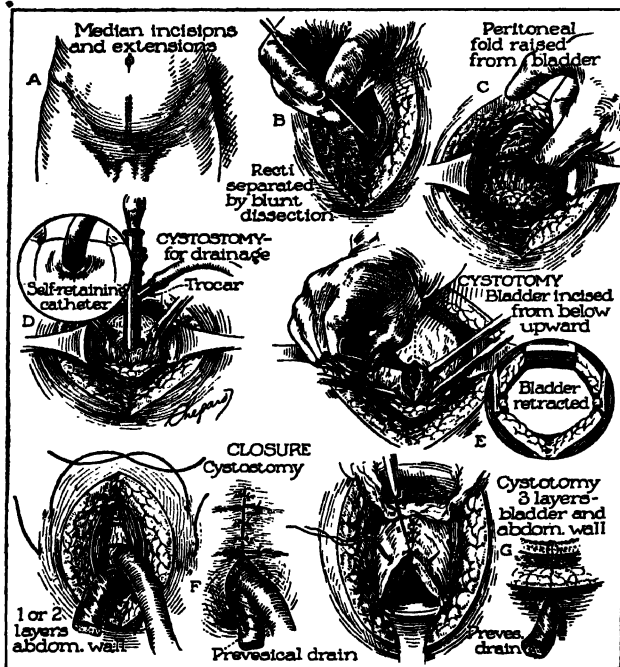
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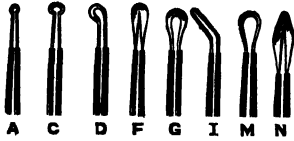
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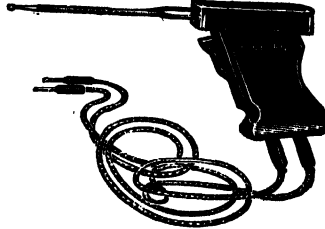
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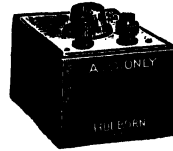


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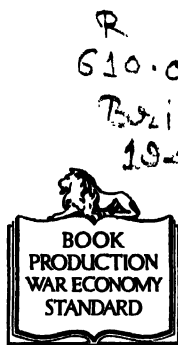
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INTRODUCTION

BY

THE GENERAL EDITOR

Medical Progress consists as before of three main sections: Critical Surveys, Drugs and Abstracts. This year there are eleven surveys, the main subjects of medicine, surgery, obstetrics and gynaecology being emphasized. We are again very much indebted to the authors who have come to our assistance and who under great difficulties have succeeded in letting us have their manuscripts at the right time. Once more the drugs section has been in the able hands of Professor W. J. Dilling; his review of the progress made during the past year in the sphere of pharmacology is as usual authoritative and comprehensive.

So far as the abstracts are concerned there are nearly 900 of these, referring to articles carefully selected from the British and American journals, the Swedish *Acta Radiologica* and the Swiss *Schweizerische Medizinische Wochenschrift*. It is hoped that by the end of another year we shall be able to record that many other European journals have been included. In some cases there has been a deliberate selection of articles which are controversial in character; the reason for this is that subscribers should be provided with unbiased opinions from catholic sources of information. As before we have attempted to make the arrangement in accordance with that of the *Encyclopaedia*, so that the classification of each abstract follows the pattern of the parent work.

The Interim Supplement to the *Encyclopaedia*, which is a separate publication appearing monthly and which seeks to supply subscribers with topical medical information extracted from current journals, has been largely referred to also in compiling the abstracts; according to plan a certain number of the abstracts printed in the Interim Supplement have been included.

H. R.

* * Since the above was written, Sir Humphry Rolleston has died. We believe it to be in accordance with his wishes that we should refrain from eulogy. There is a simple epitaph, however, which will for all time remain in our publishing house: 'The Rolleston Tradition survives'.

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GENERAL MEDICINE

By C. BRUCE PERRY, M.D., F.R.C.P.
PROFESSOR OF MEDICINE, UNIVERSITY OF BRISTOL

During the year no phenomenal advance has been made in any special subject but there has been steady progress on all fronts.

THERAPEUTICS

Penicillin

Perhaps greatest interest during the year has been aroused by the reports of the therapeutic success of preparations from various moulds which have distinctly anti-bacterial properties. At the moment the most notable of these preparations is penicillin, which is derived from *Penicillium notatum*. In 1928 Fleming, when working with certain colonies of staphylococcus, noted that in cultures which had been accidentally contaminated by *penicillium* there was marked inhibition of the staphylococcal colonies around the mould. It was soon found that this action was exerted only against certain bacteria and for some years the sole importance of *penicillium* was that it was used by bacteriologists in selective culture media. These media inhibited the growth of some organisms but had no effect on others and thus allowed the isolation of special bacteria from contaminated material. Florey and his collaborators took up the study of bacterial 'antibiotics' in 1938 and it soon became clear that the value of penicillin—as Fleming had called the active substance—exceeded the wildest therapeutic dreams. Its anti-bacterial activity against streptococci was found to be exerted in a dilution of 1 in 50,000,000, yet one thousand times the effective therapeutic concentration can be produced in the blood without any ill effect. At the same time its action, which is probably bacteriostatic rather than bactericidal, is exerted equally well in serum, blood or pus. In this it differs greatly from the sulphonamide group of substances.

Penicillin is absorbed from the alimentary canal but its use by this route is made ineffective by the fact that it is destroyed by the hydrochloric acid of the gastric juice. Rectal administration is likewise ruled out, since the drug is destroyed by the bacteria which normally inhabit the rectum and the colon. It is therefore essential when treating systemic infections to administer the drug intramuscularly or intravenously. Further, penicillin is very rapidly excreted by the kidneys and, in order to keep up an adequate concentration in the blood stream, repeated injections are necessary. At the present time these are usually given every three hours. On the other hand, when it is applied locally to infected wounds and burns penicillin has proved to be not only extremely valuable but also more economical in use, as much smaller amounts are required to be given.

Up to date the drug has not been synthesized and therefore all supplies have to be obtained from the mould. The process by which the drug is obtained is of a highly skilled and tedious kind and great care has to be taken to avoid contamination of the cultures. Various attempts have been made to manufacture 'home-made' penicillin for local application by means of growing the mould on dressings which are subsequently applied to the wound. The practice has undoubtedly been successful in some hands but it is clearly fraught with great danger.

The difficulty of manufacture has led to the preservation of all available supplies in Great Britain for use in the Forces or in special research units. At this stage of the war, with the great risk of the occurrence of infected wounds in the Forces, no objection can be raised to such procedure. In the United States of America, however, production appears to have been on a larger scale and, to judge from the reports in the journals, penicillin is available at least to some civil practitioners. In Great Britain as far as the ordinary civilian is concerned the drug remains, in the words of *The Lancet*, 'unequalled but unobtainable'. It must be emphasized again that penicillin is not effective against all organisms. Among the more important bacteria which are sensitive to the

drug are *Staphylococcus*, *Streptococcus haemolyticus*, most strains of *Streptococcus viridans* and of non-haemolytic streptococci, *Pneumococcus*, *Meningococcus*, *Gonococcus*, *Corynebacterium diphtheriae*, *Bacillus anthracis* and *Clostridium welchii*. On the other hand the typhoid, paratyphoid, dysentery and coli groups of organisms, the tubercle bacillus, *Haemophilus influenzae*, Friedländer's bacillus, *Vibrio cholerae* and *Bacillus pestis* are all insensitive to penicillin, and so are all the yeasts and moulds.

Clinically remarkable successes have been achieved in streptococcal and staphylococcal septicaemias. It has been shown that a concentration in the blood of about 1·5 units of penicillin per 100 cubic centimetres is much more effective in antistreptococcal action than are 5 milligrams of sulphadiazine per 100 cubic centimetres. (The purest material obtained at Oxford up to the present time contains about 1,000 units per milligram.)

The most remarkable results of penicillin therapy have probably been seen in cases of sulphonamide-resistant gonorrhoea. For example in one series in which seventy-two of seventy-five patients were treated by sixteen doses of 10,000 units each given intramuscularly every three hours, clinical and bacteriological cure was obtained in forty-eight hours. Of the three cases which were unsuccessfully treated, one patient could not be properly examined at the time of the report and in two reinfection could not be excluded.

Localized pyogenic infections such as skin lesions, conjunctivitis, infected burns and surface wounds have been treated by local applications with striking success. In a series of war wounds treated in this way at a forward base hospital, it was found that the largest wounds healed completely in about half the usual time and that scarring was considerably reduced.

Patulin.—Much interest and speculation was aroused by the report in November 1943 that a substance, patulin, which had been isolated from *Penicillium patulum*, when applied to the nose was followed by a dramatic recovery from the common cold. Hopes were damped however when the next week a report on the similar treatment of a hundred cases, with a hundred untreated controls, showed that there was not any significant difference between the two groups. Much more work will therefore be necessary before patulin can be hailed as a long-sought cure for the common cold.

The sulphonamides

In the field of chemotherapy, as far as sulphonamide compounds are concerned the superiority of the effect of sulphathiazole and sulphadiazine over that of other compounds on the majority of infections susceptible to sulphonamide treatment has been established. The low toxicity and high therapeutic efficiency of the compounds make them the substances of choice in the treatment of pneumonia, generalized haemolytic streptococcal infections, gonorrhoea and meningococcal meningitis. The value of the relatively insoluble compounds—sulphaguanidine and succinylsulphathiazole (sulphasuxidine)—in the treatment of bacillary dysentery has been firmly established in North Africa. A noteworthy extension of the work with sulphasuxidine has been its use locally in war wounds. It is claimed that the application of ordinary sulphonamides to large absorbing surfaces such as those of extensive burns and large war wounds may lead to a dangerous concentration of the drug in the blood. When sulphasuxidine is used however the rate of breakdown into free sulphathiazole is so slow that there is no risk that it will be absorbed in dangerous quantities into the blood stream. Its use effectively controlled wound infection with Gram positive organisms and no toxic effects were noted.

Prophylaxis.—Sulphonamide compounds have also been used in prophylaxis. An epidemic of scarlet fever which occurred in a naval station was successfully controlled by means of the administration of 1 gramme of sulphadiazine daily to all exposed men. What appears at first sight to be a dangerous experiment is the prolonged administration of sulphonamides to children with quiescent rheumatic heart disease in an attempt to prevent the occurrence of haemolytic streptococcal infection which is believed to initiate a rheumatic relapse. Further studies which were made on these lines in the United States have confirmed the original observation that there is a striking reduction in the incidence of rheumatic relapses among children who have been thus treated as compared with the incidence among untreated controls. With regard to the possible prevention of acute rheumatism by means of a more direct attack the work of Coburn and Moore is of great interest. These workers found that there was a close relation

between susceptibility to rheumatic fever and inadequate feeding, and that children in a home for diseases of the heart who were given a diet reinforced by four eggs a day did not have rheumatic relapses despite the fact that haemolytic streptococcal infections developed in some of them.

Sulphanilamide chemotherapy has also been used in prophylaxis against gonorrhoea. In a fort manned by negro soldiers every man was given 2 grammes of sulphathiazole when he left the fort on pass for the evening, 2 grammes when he returned to barracks at night and 2 grammes the next morning. This procedure resulted in a decrease in the incidence of gonorrhoea from 171 per 1,000 to 8 per 1,000; the incidence of chancroid decreased from 52 per 1,000 to 6 per 1,000.

Cold therapy

Another interesting therapeutic advance has been the gradual realization of the value of cold in the treatment of certain conditions. Cooling was first used in the treatment of gangrene and of pre-gangrenous states due to peripheral vascular disease. Its use was based on the principle that it is desirable to keep as low as possible the metabolic rate of tissues which are in an ischaemic condition. The use of dry cooling on the same basis has now been extended with beneficial results to the treatment of immersion foot. Patients with this distressingly painful condition soon noted that warmth greatly increased the pain; the therapeutic use of cold was found not only to relieve pain but to promote recovery and healing. Cold has also been used in surgery as a means of local anaesthesia, particularly in the amputation of limbs which were the site of ischaemic gangrene in old and debilitated patients. The limb is removed after refrigeration has been in process for some hours, no other anaesthesia is necessary, and it is claimed that shock is reduced to the minimum.

Venereal disease

Syphilis.—Apart from the treatment of gonorrhoea by administration of penicillin and its prophylaxis by means of chemotherapy, which is discussed above, most of the interest in the field of venereal disease has centred on the intensive therapy of syphilis. War conditions make rapid and efficient treatment of acute syphilis particularly desirable as patients are likely to be moved away from a given area at any time. Much experimental work on these lines has been conducted in the United States and to a lesser extent in Great Britain. The drug used in the experiments has usually been dichlorophenarsine hydrochloride U.S.P. (3-amino-4-hydroxyphenyl-dichloroarsine) or the closely allied mapharsen. In some cases administration of the drug has been combined with fever therapy. It has been claimed that the total curative dose for an average man is about 1,500 milligrams of mapharsen, and that this is independent of the number of times the injection is given or of the duration of treatment. The risk of the treatment is in close relation to the rapidity with which the drug is given. For instance Eagle and Hogan found that when 1,200 milligrams were given by intravenous drip in five days the fatality rate was 1 in 200 and serious intolerance developed in 1 per cent of the cases. If the same dose however is given in daily injections for six weeks the fatality rate decreases to less than 0.1 per cent. The two most serious complications are granulocytopenia and encephalitis. Jones and Maitland treated a hundred cases of early syphilis successfully by giving daily doses of mapharside for thirty days up to a total of 1,200–1,800 milligrams. In this series only one case of agranulocytosis occurred and the patient recovered when pentnucleotide was administered; there were however eleven cases of jaundice. Massive treatment is clearly still in the experimental stage and the most effective standard of dosage has yet to be determined. The War Office has not recommended intensive arsenotherapy as a routine treatment for British soldiers.

INFECTIVE DISEASES

Acute infective hepatitis

The work of Dible, McMichael and Sherlock on the pathology of acute infective hepatitis (catarrhal jaundice) studied by means of aspiration biopsy of the liver, has precisely established the nature of the lesion. It is essentially an acute hepatitis, and there is no longer room for any doubt that there is a possible catarrhal occlusion of the bile-ducts. Dible and his co-workers found that the lesions may be diffuse, zonal or

mixed and that in cases in which the jaundice lasted for more than two weeks the zonal form was usually found. Further, their work showed that there is no histological difference between the lesions of epidemic hepatitis and those found after arsenotherapy and the giving of serum inoculation. From the study of an epidemic involving three hundred cases Ford estimates the incubation period of the disease to be at least thirty-six days. Voegt attempted to transmit the disease to four persons by means of the administration to them by the mouth of 5 cubic centimetres of duodenal juice from a patient with epidemic hepatitis. After nearly four weeks all exhibited signs of hepatic impairment and one had 'subicterus' of the skin and sclera. This work although not conclusive is suggestive that the disease was transmitted in such a way. Cameron injected 1 or 2 cubic centimetres of 'infected' blood or serum intramuscularly in seven volunteers. One was transferred to another unit and was not traced. Of the remainder, jaundice developed in one a month after injection, in one within two months and in the other four within six months. It is suggested that in the last four cases the onset was delayed until the hard conditions of field service rendered the men susceptible to the disease. Findlay and Martin instilled into the nares of three volunteers nasal washings from three patients in the early stages of a hepatitis which ensued after yellow fever immunization. Jaundice developed in all three within twenty-eight, thirty and fifty-six days respectively. The symptoms were similar to those of infective hepatitis. The relation however between the jaundice which sometimes develops after injection of homologous serum or plasma (as in yellow fever immunization) and infective hepatitis is still obscure, since the jaundice does not occur after serum injection until from two to four months have elapsed. It is suggested in a *Lancet* Editorial² that the discrepancy may be explained in three ways as follows.

(1) The jaundice which appears after arsenotherapy, after the injection of homologous serum and after acute infective hepatitis is due to one and the same virus. Immunity which has been acquired in childhood usually persists but may be broken down by the direct inoculation of the causative agent, in the presence of other secondary predisposing factors.

(2) Different agents may produce the same clinical picture but immunity to one agent does not afford any protection against infection by another.

(3) The causative agents may be antigenically related but infection by one does not necessarily give complete protection against others. Hepatitis may develop if resistance is lowered by a deficiency of some essential factor or by the injection of a toxin.

Primary atypical pneumonia

In the first instance the diagnosis of this condition was largely a radiological one, and the condition was described as 'pneumonitis' and 'acute interstitial pneumonia'. More detailed study has now revealed a fairly clear-cut clinical picture. Epidemics of some magnitude have been reported. The nature of the infection is as yet uncertain but is believed to be of virus type. Similar conditions have been noted in known virus diseases such as psittacosis and lymphocytic choriomeningitis. Study of an epidemic which occurred in a barracks in Missouri suggests an incubation period of from seven to fifteen days. The few fatal cases which have been studied showed an interstitial broncho-pneumonia in which the alveolar septa were infiltrated with mononuclear cells which were also found in the alveolar exudate. The bronchial exudate contained many polymorphonuclear leucocytes.

The onset of primary atypical pneumonia is usually gradual and resembles that of 'influenza'; after from two to five days a troublesome cough develops, with retrosternal soreness and pain and occasional haemoptysis. Headache is often severe. Pleural pain is uncommon and there is little dyspnoea or tachypnoea. Physical signs are few and the temperature usually falls by lysis within from seven to ten days. Fever however may be prolonged. The X-ray picture shows woolly areas of consolidation varying in size up to almost complete involvement of a lobe. These areas may be scattered and multiple and the hilar shadows are increased. Some cases may easily be confused with cases of pulmonary tuberculosis; the picture changes rapidly and in the majority of cases has returned to the normal within twenty days.

Although the exact nature of the infection is not determined it is possible that many cases of apparent acute upper respiratory infection or of that popularly termed 'influenza' may actually have such changes. Kennedy during routine mass radiography

found 100 cases of transient pulmonary shadows in persons who had recently had a common cold or sinusitis.

CARDIOVASCULAR DISEASES

Bacterial endocarditis

This is a disease with a termination almost invariably fatal. Despite the fact that hopes were raised by the advent of chemotherapy the outlook is still gloomy. In one type of case however the position has been completely reversed by surgical treatment. In about a quarter of the number of patients with a patent ductus arteriosus bacterial endocarditis ultimately develops at the site of the patent ductus. Surgical closure of the ductus was first introduced in an attempt to reduce the risk of this fatal complication, and also to improve the general physical development of the patient which in a certain proportion of the cases is retarded. Gross reports operations on fifty such patients with only two deaths. The most striking results of the operation have been in cases in which infection had already taken place. Touroff reports eight patients operated on with five cured, and Bourne has described six cases submitted to operation in five of which there was a cure. Although the desirability of the operation in uncomplicated cases must be regarded as *sub judice*, it is clear that all patients in whom bacterial endocarditis develops should be submitted to operation without delay.

NERVOUS DISEASES

Myasthenia gravis

One of the most noteworthy of recent advances in neurology is the result of removal of the thymus gland in cases of myasthenia gravis. It has long been recognized that abnormalities of the thymus gland often appear in myasthenia gravis; tumour or obvious hyperplasia has been found in over half the number of cases examined at necropsy. Attempts to cure the disease by removal of the gland meet with varying success. Brain reports three cases which do not show any improvement; Carson had three post-operative deaths, three patients cured and three not improved out of nine cases subjected to operation. McEachern had analysed the relation between the thymus gland and myasthenia gravis and tabulates fourteen cases in which the patients were subjected to thymectomy. Four died as the result of the operation but of the survivors all showed some improvement and some were cured. The operation is clearly hazardous and not to be undertaken lightly, especially as at present there is not any method of determining beforehand whether or not the patient in any given case is likely to benefit.

PSYCHIATRY

Prefrontal leucotomy

In the field of psychiatry much interest and speculation has been aroused by the operation of prefrontal leucotomy which was first introduced in 1936 by Moniz of Lisbon. A considerable number of cases have now been subjected to the operation in Great Britain. McKissock reports a mortality rate of less than 5 per cent and it is surprising that very little evidence of severe damage to the higher intellectual faculties can be demonstrated after operation (Editorial, *Lancet*¹). There is general agreement amongst those who have had experience of the operation that it does not specifically cure any precise type of mental disease. It does produce a state of mild euphoria and a decrease of emotional tension, and thus symptoms associated with apprehension, emotional tension and agitation tend to diminish. For instance an impulsive and violent schizophrenic may show remarkable improvement, and an obsessional syphilophobe although he may still believe that he is suffering from syphilis is no longer worried by or even interested in his condition.

ENDOCRINOLOGY

Pituitary extract

In the realm of endocrinology two therapeutic advances are reported, of which one is the preparation of a slow-acting pituitary (posterior lobe) extract. One of the difficulties in controlling diabetes insipidus in the past has been the need for often repeated injections. Attempts to prolong the action of pituitary extract by an emulsion in oil were disappointing—the injections commonly gave rise to paraffinomas at the site of injection. More recently however the use of pituitary tannate in oil has been very successful. No ill effects have been noted after many injections and the number of

injections required is reduced to a third or a quarter of the number needed when ordinary pituitary extract is employed. This is an improvement of no slight importance to the sufferer from diabetes insipidus, and one closely parallel to the improvement in treatment that was a result of the introduction of the insoluble insulins. It is probable that the introduction of similar insoluble preparations of other hormones will increase considerably the efficiency of endocrine therapy.

Thiourea and thiouracil

The promise of a real medical cure of thyrotoxicosis is held out by the report of treatment of this condition by thiourea and the allied substance thiouracil. The surgical treatment of thyrotoxicosis although it is of very great value can never be completely successful since it is clear that the thyroid gland itself is not primarily at fault. It appears that thiourea and thiouracil exert their effects not by neutralizing circulating thyroxine but by inhibiting its formation. Although their use at present is in the experimental stage it is clear that the effect of their administration takes from two to three weeks to become evident, and that use of one drug or the other has to be continued for a long time by means of a maintenance dose. Whether or not this may be gradually reduced and finally stopped altogether is not yet known. The drugs are not free from danger; thiourea may cause nausea and vomiting and a troublesome conjunctivitis, and thiouracil has produced a serious granulocytopenia.

CHILDREN'S DISEASES

Primary tuberculosis

In the study of children's diseases one of the outstanding recent developments is the increase in clinical recognition of primary tuberculosis in children and of its importance. The report of the British Paediatric Association on this subject points out the methods of clinical investigation by which the diagnosis may be established. It is clear that in Great Britain tuberculin tests should be far more often employed than has usually been the case. Further, if the cases are to be dealt with adequately a form of hospital or convalescent home accommodation is necessary in which education can be given to the older children. Sanatoria are considered to be undesirable places for these patients on account of the possible risk of reinfection. Again, the notification machinery needs to be overhauled. Primary tuberculosis occurring in children is often an indication that there is an adult contact who has pulmonary tuberculosis, and it is therefore important that children so affected be brought to the notice of the persons responsible for detecting tuberculous disease. On the other hand it is not considered desirable that such children should be labelled 'tuberculous'. Many—in fact the majority—should make a complete recovery; if they are to be reported as cases of tuberculosis it might be argued that every adult who gives a positive tuberculin reaction should be dealt with similarly.

The grave nature of primary tuberculosis when it occurs in young children has been emphasized by Fleming who shows that nearly a third of the number (92 of 286) of children under four years of age who were found to have a positive tuberculin reaction were suffering from tuberculous meningitis. He points out that in at least 75 per cent of cases of tuberculous meningitis in children the disease arises from a pulmonary primary complex, which means infection by inhalation from a human source. Fleming insists upon the need to protect young children from infection as far as it is possible to do so.

INFANT FEEDING

Lactation

Of considerable importance to the paediatrician is Waller's study of the control of lactation. As a result of his observations he postulates a reflex mechanism which governs the outflow of milk from the breast. He suggests that the failure of breast feeding so common during the second or third week—although the mother often says that she 'had too much milk at the start'—is due to frustration of this 'draught' reflex by over-distension. If this theory is correct, it lays emphasis on the need (1) for putting the baby to the breast early, (2) for feeding from both breasts at each feed and (3) for suckling in the early stages at least every three hours.

VITAMINS

The separation of the vitamin B complex into different components led to a search for the clinical picture of each separate deficiency. Thus pellagra was believed to be due to nicotinic acid deficiency and beri-beri to aneurine deficiency; ariboflavinosis was said to give rise to cheilosis (angular stomatitis), magenta-coloured smooth tongue and keratitis. Further studies have shown that the amount required of each fraction of the B complex is in part dependent upon the amount of the other factors available. Experimental studies with riboflavine-deficient diets which have failed to produce the clinical picture expected, and the fact that the described symptoms have failed to respond to riboflavine therapy, have thrown still more doubt on the subject of vitamin deficiency as a whole. It is clear that much more study is necessary before the interrelation of the various units of vitamin B and the clinical manifestation of their deficiency can be fairly established.

EXPERIMENTAL MEDICINE

Two eventful discoveries which have been made in the field of experimental medicine must be mentioned.

The first is the experimental production of necrosis of the islands of Langerhans in the pancreas, with subsequent development of severe diabetes mellitus, as the result of the administration of alloxan. This is an oxidation product of uric acid and when injected into animals may produce a fatal hypoglycaemia. If however a series of smaller injections is given to rats, hyperglycaemia, glycosuria and all the symptoms of severe diabetes mellitus develop. Post-mortem examination reveals a selective necrosis of the islet cells. Thus there is now available a relatively simple method by which a condition almost identical with human diabetes mellitus can be produced in animals. This should make much easier the study of the human disease.

The second advance in experimental medicine is the claim by Bacon to have produced immune serums artificially. Plasma, while undergoing a process of dehydration, was treated with an antigen such as diphtheria toxin. After treatment the plasma was restored to its original volume by the addition of distilled water. The reconstituted plasma was then tested for antibodies by the addition of the toxin, with the result that a precipitate, believed to be antigen antibody precipitate, was formed. The work must be confirmed and extended before the claims made can be substantiated, but it opens up a fascinating realm of speculation.

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SURGERY

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The literature of war surgery is now becoming bewildering and it is more than ever necessary to regard studiously the underlying principles which have been gradually built up as a result of the experiences of many wars.

SURGERY OF WAR-TIME

In the expedition of Belle Isle, John Hunter observed that the effect of cannon fire was much more serious when damage was done to the hull of the ship and its contents for thus secondary missiles were created and the possibilities of casualties were multiplied (Paget¹). It was Guthrie, when he was serving in the Peninsular wars of 1808-15, who settled for all time the principles underlying the treatment of secondary haemorrhage. His *Commentaries* are full of valuable lessons and are fascinating and pertinent reading even at the present time. Some of the younger surgeons are inclined to be a little critical because methods that were recommended in connexion with the recent North African campaign are now being superseded since the fighting has been transferred to Italy and elsewhere. The fact merely emphasizes the importance of the differences in types of warfare, for instance close-in fighting with small-arms is bound to be very different from fighting in wide open spaces where for the most part the arms are long-range artillery and bombing aircraft. But in addition to the type of warfare and the type of missiles the actual battles play a part. The nature of the terrain is most important, as we soon found to our cost in the campaigns over the heavily cultivated soil in Flanders in the war of 1914-18 as compared with battles on the open veldt in the South African war in the early part of the century. All the time, surgeons who may have already become veterans in the present war are learning, and not only from their own changing experiences but also from the interchange of experiences with those who have worked in other fields, and to a more limited extent from the interchange which is going on between the Allies. One officer in commenting upon his war-time experiences in more than one field was very emphatic about the extreme importance of transport, which many, dating from the time of Baron Larrey, Surgeon-in-Chief to Napoleon's *Grande Armée*, have regarded as the key to the whole situation. The testing of various methods in detail is largely a question of observation in the quieter times when medical officers are working under more static conditions and are not overwhelmed, for it is not usually in the greatest and fiercest of battles that the most useful experience is gained. Many, as might be expected, are critical of methods of wound treatment which are tested on experimental animals. This method of investigation is valuable to an extent only very limited when compared with the abundant opportunities for clinical research which warfare provides.

Considerations of the same kind apply to the question of the bacteriology of wounds. There it is as well to remember that in actual warfare this matter is intimately connected with the soldier's environment. This is exemplified in personal hygiene and involves such matters as change of clothing, facilities for washing and attention to the bowels, as well as the stage in the struggle at which the wound has been inflicted, for exhausted men have not the resistance of those who are fresh and well fed. In bacteriological investigations it is not enough simply to recognize that a certain organism has been responsible for an infection; we require to know more of the type of the particular organism, the degree or weight of the infection, the evidence of body resistance and so forth. This has been partly worked out by the study of blood cultures and it has

been found, for instance, that a positive blood culture of some strain may not be of any great value in prognosis or in management, whereas the numbers of colonies which grow in a stated time in suitable media are an indication which may be of great value of the heaviness or otherwise of the infection (Butler).

It is always well to remember that in all probability the defences of the body play a varying part. At one stage, for instance, organisms may be circulating in large numbers in the blood stream whereas at other times they may be very thinly represented. This may be due either to the fact that floods of organisms invade the blood stream at different times or that the organisms multiply in the circulating fluid or that the defences of the body may at times be sufficiently vigorous almost to dispel them from the blood stream. Reflections of this sort lead to consideration not only of the organism but of the host or, to put it another way, not only of the quality of the seed but of the soil. This aspect of the matter has been recognized ever since bacteriology was known but it is apt to be overlooked. During the war of 1914-18 Crile, among others, made observations on wounds with regard to the conditions of the soldier at the time of wounding; it was found that in the early stages of what looked as if it were going to be a successful battle the infections were not as serious as were those that occurred in a later stage of a conflict in which it seemed as if the cause were nearly lost and when the resources of the patient were worn out by the magnitude of his exertions. 'The soldier is fresh and keen when the Germans attack him—he is depressed when the bacteria attack him.' Accounts of war wounds are sometimes spoken of as though missiles were selective, whereas a moment's consideration would show and very little experience must teach that no such generalization can be made. One of the most remarkable things is the occasional apparent vagaries of some small fragment and the almost unheard of injury which sometimes may be caused by its passage through the tissues. In this way we already have knowledge of injuries in which the oesophagus has been the most important structure damaged, in which the thoracic duct has been divided, or in which some other important structure has been apparently selected for injury, whereas others near by have escaped. Missiles may be diverted however in an extraordinary way by structures of varying density, by bony prominences, by cellular planes and by the elasticity of structures such as blood vessels. It is remarkable that the trunk or a limb may sometimes be traversed by a missile without serious damage when the direction of the track would suggest that important vessels and nerves could not escape injury. One of us (Grey Turner) has always insisted that a great deal can be learned by careful and detailed examination of casualties occurring in quiet times and he constantly urged that every opportunity should be made to use such occasions for acquiring a knowledge of the possibilities of the damage which can be caused by missiles of various kinds and in various situations; when opportunity offers such clinical examinations should be followed by careful post-mortem examinations.

These general matters are not only of interest but also of practical importance, yet when all is said and done 'Difficulties of course remain that experience alone can solve and when not to operate and when not to evacuate are among the most striking' (Blackburn). Many factors have been operative in bringing about the better results which generally speaking so far have followed the treatment of the wounds of the present war as compared with those of the war of 1914-18: early excision, the use of sulphonamides and more recently of penicillin, tetanus toxoid prophylaxis, early plaster fixation, specially trained mobile surgical teams and, for the most part, healthier environment than the tetanus-ridden mud of Flanders provided.

It must not be forgotten however that there is another important factor in the character of the wounds themselves; this depends upon the nature of the missile and the velocity imparted to it. For the most part the wounds of the present war have been caused by small fragments which are comparatively light, intensely hot and travelling at velocities of a magnitude which never before has been attained. In consequence such fragments tend to penetrate cleanly the body coverings, uniform, equipment and so forth which they strike, and once they have done so their momentum is changed rapidly and they come to rest after a comparatively short distance. Compare this with the leaden musket-ball which mortally wounded Nelson. It entered over the left shoulder, traversed the spinal canal in the mid-thoracic region and came to rest in the muscles of the back on the opposite side of the body. When the ball was removed there was found firmly attached 'a portion of the gold lace and pad of the epaulette, together, with a small piece of his lordship's coat'. In the war of 1914-18 it was common to

find such objects as pieces of uniform, webbing or leather equipment in wounds and although such has occasionally been the case in the present conflict, wounds for the most part would appear now to be less contaminated by this means, especially those wounds produced by fragments of bomb or shell. Numerous cases have occurred in which X-rays have revealed in the brain small pieces of bomb or shell fragments, of which it has been hard to detect the entering wounds in the scalp, so small and clean have they been, and it has been exceptional for hair, pieces of scalp or calvarium to be indriven with such fragments, the great majority of which have remained surgically clean and have not produced any evidence of infection. This factor of the changing character of wounds must be given due consideration when we take into account the results of present treatment as compared with that in past wars in which different weapons and missiles were used (Rogers). As the war proceeds answers are forthcoming to certain specific problems, for instance general agreement seems to have been reached on the treatment of wounds of the large bowel. In these serious injuries exteriorization after excision or even without it gives much better results than does any other method and has reduced the immediate mortality by half.

TREATMENT OF WOUNDS AND OTHER LESIONS

Penicillin and war wounds

At the moment great interest is focused on this substance and those who have lived long in the practice of surgery have the fear that some of the extravagant expectations about its virtues may be in the proof disappointed.

During 1943 penicillin was taken to the Mediterranean theatre of war and reports of the results of its application have recently come to hand (War Office Memorandum). It was necessary to ascertain the best and most economical methods of its use in prevention of sepsis under battle conditions. It has been found that in addition to the beneficial effects of early instillations of penicillin in wounds, with it infection in compound fractures under fourteen days old can sometimes be brought under control. In adequate dosage the substance proved to be effective against gas gangrene but did not counteract the toxæmia; all dead muscle therefore should be excised and anti-gas gangrene serum should be given in large doses. Bacteriological examination of material aspirated from brain wounds showed in the majority of cases that with penicillin Gram positive cocci disappeared from the wound within forty-eight hours. All who actually did the work in North Africa insist that although penicillin is a strikingly valuable substance in the treatment of infection it does not replace surgery and that the ordinary canons must be observed—such for instance as the removal of dead or of grossly contaminated tissue, adequate provision for drainage, immobilization of severely injured parts and so on. Penicillin has also been used with success in infected burns and surface wounds, as well as in such hitherto troublesome cases as osteomyelitis of the frontal bone (Williams and Nichols). Experience so far encourages the hope that bone infections, if treated early, may recover without the formation of sequestra (Robertson). On the other hand, in the presence of sequestra its use is unlikely to give bacteriological control (Mowlem).

In the battles in North-West Europe penicillin was tried extensively as a prophylactic against sepsis and gas gangrene. A War Office Memorandum recommended that it be administered by intramuscular injection in an initial dose of 90,000–100,000 units with a maintenance dose of 45,000–50,000 units in 6 hours and thereafter every 5 hours until a hospital was reached in which complete surgical treatment could be carried out. The results obtained with penicillin may be said to be encouraging. Wounds are doing much better, primary suture is often possible, the period of healing has been reduced by between three and six weeks and the necessity for amputation is often averted. There is always a danger that, with new antiseptic substances as with new drugs, we may expect too dramatic results or may tend to rely too much on the new preparation, forgetting the ancillary circumstances associated with its use. Reports however are most encouraging and the surgical world awaits only supplies and guidance concerning the optimum doses and the methods of administration. Among combinations which may soon be rendered superfluous by the use of penicillin is the sulphathiazole-proflavine powder, ratio 99 : 1, which seems to have given very satisfactory results (Feggetter).

Chinosol and refractory infections

There is now a constant search for those chemotherapeutic drugs which are inimical to special infections and which can help to eradicate such infections even when they have become chronic and to prevent the late recrudescence of infection which is so much of a nuisance and bugbear especially in cases of bone injury.

In the North African campaign most troublesome and refractory infections often developed in connexion with small wounds, abrasions, insect bites and so forth and sometimes it was found that the reason was inoculation with the organisms of diphtheria. The causation having been established it was disturbing to find that the infection did not respond to the use of antidiphtheritic serum such as we have been accustomed to rely on in Great Britain. In these circumstances chinosol (potassium hydroxy-quinoline sulphate), one of the older antiseptics, has proved to be valuable. This substance is said to inhibit the growth of the diphtheria bacillus in culture in very weak dilutions but as a dressing it can be used in the strength of 1 in 1,000 (Mangabeira-Albernaz; Killian).

Effect of vitamin C on wound healing

Although it is not perhaps sufficiently realized that adequate amounts of vitamin C are necessary for the effective healing of wounds, the evidence for the fact is considerable (Bourne). As supplies of the vitamin are not being obtained from natural sources as abundantly as they were before the war, the desirability of administering adequate amounts of ascorbic acid to patients in whom there is likely to be a deficiency is manifest. In most campaigns the nutritional state has had much to do with the healing of wounds but its importance has not always been realized. The story of Ambroise Paré and the 'great pot' (Paget²) should ever be in the mind of the army medical officer. It is not only the quantity or the quality of the food that matters but also the variety. The common-sense regulation of diet (as far as it can be controlled on active service) is all part of the now fashionable art of rehabilitation.

Nerve and tendon injuries

Four considerations are of paramount importance for securing good results (Koch). (1) Healing of the operation wounds by primary union. (2) Operation must be so carefully performed that nerves and tendons heal with a minimum of inflammatory reaction and hence of subsequent scarring. (3) The affected part must be kept at rest in such a position that there is a minimum of tension on sutured nerves and tendons until sound healing has taken place. (4) If nerves have been sutured the muscles supplied by them must be supported in a relaxed position until regenerating nerve fibres have made their way to the periphery, as indicated by Tinel's sign. [In order to elicit this sign the course of a nerve is lightly percussed with the tip of the finger or a patella hammer from below upwards; when the level to which regeneration has occurred is reached, a sensation of tingling is experienced. It has proved to be of the greatest value both before operation in determining the site of the lesion and after operation for following the progress of regeneration.] At times it is often impossible to determine without operation whether or not peripheral nerve injuries which are the result of gunshot wounds are complete. If there are no signs of recovery within six or eight weeks the nerve should be explored. Neurolysis should always be tried when there is doubt about the advisability of resecting the lesion. Ballooning of the nerve into which saline had been injected by means of a very fine hypodermic needle was extensively used in the war of 1914-18 and is again recommended by Norcross. Combined with incisions into the nerve in order to relieve tension in the scar, the procedure has in some cases produced excellent results. In one hospital in which 100 operations on nerves had been performed, roughly a third of the number of operations were for complete severance and comprised end-to-end suture; the remainder were for incomplete injuries and consisted of neurolysis. Good results were claimed in 80 cases (Walters).

Vascular injuries

Only very rarely can there be an opportunity of carrying out primary repair of a main blood vessel which has been damaged by gun-fire and as a rule ligation of the trunk is necessary. What can be done to reduce to the minimum the disturbance to the peripheral circulation which must follow such ligation, and what to encourage and assist the establishment of an efficient collateral circulation? The following procedures have been suggested.

Division of artery.—The artery should be divided between ligatures and not merely tied in continuity. The advantages are as follows. (1) The dividing of an artery interrupts the peripheral vasoconstriction reflex which follows damage to the vessel wall. (2) Ulceration with consequent secondary haemorrhage is less likely to be present at the site of ligation, at which erosion of the vessel wall is always a danger when a large artery is tied in continuity. Complete division permits complete contraction and retraction (shortening) of the vessel due to its elastic elements. This produces a thickened wall at the site of the ligature and a firmer occlusion. (3) If tied in continuity the vessel lumen may become re-established.

Simultaneous venous ligation.—Despite varying opinions, experiments have shown that if the vein as well as the artery is tied the peripheral circulation suffers less (Holman). The Russian surgeon Oppel suggested the procedure before the war of 1914–18 and Sir George Makins was so convinced of its value that he caused an Army Order to be issued in respect of it. Holman lays down that if the distal end of a main artery does not bleed well when the ligature on it is temporarily released, the vein should be ligatured. If the distal part of the artery spurts bright blood the vein may be left untied.

Paravertebral sympathetic block or ganglionectomy.—This will remove any remaining spasm in the distal vessel and its branches.

Blood transfusion.—German surgeons (Bartholomé) have found in the present war that if ligature of a main artery produced extreme pallor indicative of impending necrosis, the rapid introduction of 800–1,200 cubic centimetres of blood saved the limb. It is suggested that this results because the increased volume of the circulating blood causes a rise in arterial pressure with an opening up of the collateral circulation.

Ice packs.—The limb may be packed in ice for several days in order to reduce its metabolism in the hope that the reduced circulation will in these circumstances be adequate during the time that a collateral blood supply is being established. This may seem to be an extreme measure but the method is being tried by several surgeons and their experience should show whether or not it has any advantage over the more usual and well established plan of keeping the limb at body temperature.

Subphrenic abscess

This is one of those conditions which are extraordinarily variable in their manifestations but there is no doubt of the major importance of the abscess in abdominal surgery. It may be primary—that is, the only evidence of infection in the peritoneal cavity—but it is more usually associated with peritonitis from which the patient is recovering. The condition is one of the commonest of the complications after ruptured peptic ulcer and should be borne in mind as a possible complication after the operation of gastrectomy. It must always be regarded as very serious—one of the principal killing complications of abdominal surgery—although in some cases the patient recovers spontaneously. It is a great mistake to suppose that the symptoms and signs are necessarily distinct and according to text-book descriptions; this applies especially to the earlier stages. Pain is not an important feature, but when the condition of the patient suggests that there is some septic mischief going on inside the abdomen and when there is just a little catch in the breath with discomfort in the lower part of the chest, the syndrome is a very suggestive one. Often at this stage the presence of a little fluid in the pleural cavity may be demonstrated and the latter may be withdrawn with the exploring needle. As a rule the fluid is quite clear and comes from above the diaphragm; it really represents the oedematous exudate round about the periphery of an inflammatory focus. At such a stage the X-ray film may show a little elevation of the diaphragm with either limitation of movement or fixity, but no considerable shadow may be demonstrated and the bubble of gas beneath the diaphragm which is so helpful may be entirely absent. The important thing is to suspect the condition and not to be too ready to attribute the symptoms to some primary pulmonary inflammatory condition. The latter condition may be serious enough although it generally tends to improve, but subphrenic collections are much more likely to become steadily worse and very often lead to the death of the patient. Many a death from subphrenic abscess has been attributed to pneumonia. When abscess is suspected the surgeon must be constantly on the alert—‘diligently searching for the cause of a stormy convalescence’ (Raw)—to discover any collection which can be located and drained. X-ray examination followed by the exploring needle is extremely valuable. When all the circumstances

point to the strong probability of the presence of such an abscess although it cannot be located by the exploratory needle, the patient should be put under general anaesthesia so that multiple punctures may be made with a wide-bore needle. The close scrutiny of life-size transverse sections of the body such as are provided in Symington's anatomical atlas are very helpful. If all efforts fail it is justifiable to open the abdomen so that the subdiaphragmatic spaces may be explored with the hand.

It must be remembered that a comparatively small abscess (containing, say, no more than two or three ounces of pus) may make a patient desperately ill. There is no doubt that some patients either get well spontaneously or are assisted to do so by chemotherapy, but this fortunate happening cannot be relied on and the well-developed condition is only likely to be cured by incision and drainage. For this purpose no one method of approach will suffice for all cases and the surgeon must be guided in his choice by the localization of the abscess. The shortest and most direct route to the surface should be the aim. If the organisms are sensitive to penicillin the use of the substance may obviate or at least reduce the extent of purely surgical procedures in such cases. The subject is a big one and is now ripe for an authoritative reconsideration in all its aspects.

Hiatal hernia

Another condition that may be of great interest and importance is hiatal hernia, which is not nearly so uncommon as it is often supposed to be. The diagnosis provides interesting problems for the general physician, the cardiologist, the oesophagoscopist and the radiologist as well as for the surgeon (Turner, J. W.). It is quite remarkable how often sufferers from this condition have either been operated upon in the expectation of finding gall-stones or gastric ulcer or have been under the care of a physician usually with the idea that they have heart block or cardiac muscle disability. Once suspected, the presence of the condition will probably be confirmed by careful radiological examination; in fact, this is the major method of confirmation of the diagnosis, for a comparatively small hernia of such a type does not give rise to ordinary physical signs although it may be a lifelong burden to a patient. The most important thing is to establish the diagnosis; the question of operation will arise only if there are definite symptoms. If surgical interference is deemed to be necessary a competent surgeon with some experience can undertake its management with considerable confidence, although the operation may be technically difficult. The abdominal exposure is usually sufficient for this particular type of hernia; mobilization of the left lobe of the liver is a considerable aid in exposure. As a concluding stage a temporary gastrostomy is undoubtedly valuable. It not only gives the surgeon the command of the dilatation of the stomach which is so apt to ensue from the operation, but also is a means of fixing the stomach until the sutured diaphragm is securely healed, for the viscus tends to slip up into its old position.

POST-WAR PROBLEMS

In these days it is not possible to separate entirely military conditions from those which exist in civil communities, for we have returned soldiers who enter civil life; furthermore there are many infections which may be transferred from the soldier to the civilian. This is a problem which will become more difficult and it is mentioned merely to remind readers that the troubles that may arise are not limited only to medical conditions, such as malaria, but will concern other diseases of importance. Amongst them are the following.

Amoebic infections

The experiences of the war of 1914-18 showed that every now and again manifestations of amoebic infestation become active some considerable time after the patient has returned to the temperate climate of Britain. The possibility of such an infection must be borne in mind in cases of unexplained or obstinate diarrhoea and of proctitis and especially in cases in which hepatitis is suspected. This is the commonest condition and it may go on to abscess formation. In cases of doubt the suspicion of a tropical origin should be aroused, for once the condition is diagnosed the resources of management are fairly wide. When amoebic hepatitis arises in Great Britain it is highly probable that the infection may be very resistant to treatment, but emetine still remains the sheet anchor in treatment. Those who have not seen much of amoebic disease may have the erroneous impression that surgery has little or no place in its management.

Peptic ulcer

Lately there has been a good deal of talk about the after-history of peptic ulcer which has come under notice because of the accident of perforation. Some readers will remember the time when it was supposed that this serious happening was often the means of bringing about a cure of the ulcer. But for long enough it has been recognized that in a very noticeable proportion of cases the patients either did not get any relief after perforation or only a comparatively short respite. Even with such knowledge it must be very disappointing to some to find that careful inquiry shows that as many as 50 per cent of the patients have recurring trouble which demands careful consideration and management (Mailer^{1, 2}). It does not follow that so considerable a number will require further operative measures; but the patients do require advice and help and those who have most to do with them will freely admit that an operation such as gastrectomy is often called for. This however is no new discovery; as long ago as 1912 Grey Turner, in the scrutiny of the after-history of what was then a fairly large group of cases which had improved after perforation, drew attention to the fact that at the best probably a third of the number of patients had subsequent symptoms pointing to reactivity of the peptic ulcer and that with a more rigid interpretation of the symptoms quite likely as many as 50 per cent had been affected in this way.

Gastrectomy or gastro-enterostomy?

The subject of peptic ulcer leads to a consideration of the later results of gastrectomy. Not unnaturally the profession is beginning to ask, 'Is this very drastic operation really justified in having—as it appears to have—almost completely ousted gastro-enterostomy from the surgical field?' It is a striking fact that in many of the big surgical clinics at the present time gastro-enterostomy is a rare operation whereas gastrectomy is so common that there are nearly always cases in the wards. It is fair to say, even without the support of statistics, that the results are better when the operation is carried out for ulcers originating in the stomach, usually of the lesser curve type, than when duodenal ulcer has been regarded as the indication. Duodenal ulcer in a youngish man with a high acid curve still remains a problem for which it is questionable whether the correct answer has yet been found. For malignant cases it ought to be stated most emphatically that, in spite of the very numerous disappointments, partial gastrectomy is by far the best palliative measure that can be employed; in many cases the amount of relief afforded by this operation is well worth while, even if, as so often happens, recurrence eventually overtakes the patient within a year or two. Conservative surgeons are now wondering about the results of total gastrectomy for cancer with its great technical difficulties and high mortality. There again the matter ought to be reviewed in relation to the alternatives, which as yet are practically useless except as measures of palliation which bring relief for very short periods. Appreciation of the position has led to a renewed interest in the possibilities of the surgical management of growths at the cardia; the technique of the management of this difficult problem by transthoracic and transdiaphragmatic resection is slowly but steadily being evolved (Phemister).

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OBSTETRICS AND GYNAECOLOGY

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OBSTETRICS

Speed and movement of spermatozoa in the human uterus

An attempt has been made to estimate the speed of human spermatozoa *in vivo* by carrying out experiments on uteri which had been removed by total hysterectomy (Brown). In each case the specimen was warmed to body heat in an incubator and was then wrapped in a warm saline compress; in three cases the uterine cavity was perfused with physiological saline. The position of the organ and its appendages was adjusted so as to simulate the normal position in the body; in short, throughout the experiments an attempt was made to reproduce natural conditions, including the normal retrograde currents in the tube. Two cubic centimetres of semen of known age and vitality were placed in a receptacle in contact with the cervical end of the excised uterus and at intervals thereafter the fimbriated end of the tube was immersed in a drop of saline placed on a glass slide, and the saline was examined for sperms. Of the six uteri submitted to examination, three gave a satisfactory result and it was found that the average time of transit from cervix to abdominal ostium was sixty-nine minutes. The average distance travelled was 18.9 centimetres (of which 10.5 centimetres represented the tube) and the average distance covered per minute was 3.5 millimetres in the uterus and 2.5 millimetres in the tube.

These experiments have shown that the human sperm reaches its destination in approximately sixty-five minutes. Brown concludes that contact between the ovum and the sperm in the human genital tract is most likely to occur about seventy minutes after the sperm has been deposited in the fornices. According to Hammond fertilization takes place only after a large number of sperms have reached the ovum. The rate of progress of the sperm must be influenced by many factors, including the length of the distance to be covered and the state and activity of the tubal ciliated epithelium and, to an unknown extent, by the morphology and vitality of the sperm itself.

Artificial insemination

Folsome has made an opportune survey of this interesting, important and controversial subject. The success of the method in animal husbandry first drew attention to the possibilities of its application to the human subject—especially the extraordinary results obtained by the Moscow Experimental Station, which had (up to 1932) impregnated successfully by artificial means no less than 2,000,000 cows, 3,000,000 ewes, 650,000 mares and 200,000 sows; 4,000 ewes had been fertilized by sperms from one ram in a breeding season of forty days. These methods had been introduced into America where artificial insemination stations had been set up at various agricultural colleges and good results had been obtained, but on a much smaller scale; nowadays their chief interest was centred in sperm physiology rather than in artificial insemination.

It was inevitable that an attempt should be made to introduce this method into the field of human reproduction, but Scanlon, writing in 1938, could find only twenty-four articles on the subject in the American literature. One may note in passing a fundamental difference between the animal and the human experiments—in animal husbandry only healthy individuals are employed and the insemination is artificial but physiological in type, whereas in the human subject the method has been applied chiefly for the relief of a pathological condition, namely sterility, when one or both of the individuals concerned in the mating are abnormal; under such conditions the insemination cannot be regarded as physiological and it is not surprising that the general results have been discouraging.

In 1941 however Seymour and Koerner published a paper in which it was claimed

that 9,489 women had achieved at least one pregnancy by this means. Folsome shows quite plainly the grave objections there are to the acceptance of figures which are approximately twenty-one times greater than those which had been reported in the entire medical literature during the previous forty years, and makes a plea for more vigilance on the part of editors in regard to the publication of papers which record sensational results but furnish no scientific proof of their accuracy.

There are two methods of insemination: (1) homologous, in which the husband's semen is introduced into the vagina or uterus, and (2) heterologous, in which the semen is supplied by a non-member of the family. The homologous method does not present any medico-legal complications or difficulties, but the results are relatively poor and it has little to recommend it. Folsome thinks that the heterologous method, whereby the wife is impregnated with semen not her husband's, may carry 'potential and devastating repercussions to the wife, the husband, the donor, the relatives and the physician'. These possibilities are not eliminated by the special technique described by Stepata, by which the donor's semen is injected into the ejaculatory ducts of the husband and passed from the husband to the wife by an act of coitus undertaken soon after the injection. It would appear that the donor might be charged with adultery or cited in a divorce action, and that the child might be declared to be illegitimate. The work done on artificial insemination has served a useful purpose because it has drawn attention to the part of the male in sterile marriages and has promoted research into the physiology of the sperm cell and the conditions which govern its survival *in vivo*.

Macleod and Hotchkiss have shown that it is possible for some males with azoospermia which is due to obstruction in the vas deferens to have adequate sperm formation below the site of the obstruction; these and similar discoveries have stimulated further research into the causes and treatment of male infertility.

Tests for pregnancy

Colostrum test.—The colostrum intradermal test for the diagnosis of pregnancy which was introduced by Falls, Freda and Cohen in 1940, is based upon the type of reaction which is produced by the injection of one-fiftieth of a cubic centimetre of colostrum obtained by manual expression from the breasts of primigravidae twenty-eight weeks pregnant. The result is regarded as positive, that is to say the patient is pregnant, if the injection does not produce any local reaction, and as weakly positive if a red areola appears but vanishes within sixty minutes. A negative (non-pregnant) result is one associated with an enlarging wheal and a surrounding red areola which persist for more than an hour; it should however be noted that the originators of the test regarded all cases as negative which showed an areola only at the end of sixty minutes.

Allen and Donaldson have reported a series of cases in which they have applied this test to both pregnant and non-pregnant women, with the following results. Of 164 women known to be pregnant, 82 tests were correct, 69 incorrect (13 were excluded as indeterminate); this gives an accuracy of 54·30 per cent as compared with the 98 per cent of accuracy obtained by Falls and his colleagues. Of 84 women known not to be pregnant, 71 gave a negative result and 10 a positive reaction (3 results were excluded as indeterminate) which shows an accuracy of 87·65 per cent compared with the 96·7 per cent of accuracy for the non-pregnant group recorded by Falls, Freda and Cohen.

Prostigmin test.—The prostigmin test, which was introduced by Soskin, Wachtel and Hechter, consists in giving 0·5 milligram of prostigmin by intramuscular injection on three successive days and noting the presence or absence of sequential uterine haemorrhage. If bleeding occurs the patient is not pregnant; if there is not any evidence of uterine haemorrhage, she is pregnant. The test does not apply to patients at puberty and the menopause, or to women with pronounced endocrine disturbances or with gross menstrual irregularity. If these classes are excluded the results are reliable and it is claimed that the method is free from all risk.

Carapetyan advocates the use of prostigmin not only as a test for pregnancy but also as a method of treatment for cases of delayed menstruation due to simple functional causes. He records the results in fifty-seven cases and claims that the thirty-four women who were not pregnant all menstruated in response to the treatment.

This method is therefore applicable in routine clinical work both for diagnosis and treatment and, provided that unsuitable cases are eliminated, the results are likely to be satisfactory.

Treatment of stress incontinence

Stress incontinence is a term which implies loss of bladder control in response to effort of any kind; in the worst cases the loss of control may be almost complete.

The chief cause of the condition is childbearing, which damages the neuromuscular apparatus responsible for bladder control either by direct injury or by subinvolution of the participating muscles; it may occur too in childless women who are the subjects of congenital defect or underdevelopment. The association of spina bifida occulta with nulliparous prolapse is significant from this point of view.

Counsellor describes twenty-six cases in which the patients were completely cured by a simple form of vaginal repair which was originally designed by Kennedy as a result of his study of the mechanism of micturition and the anatomy of the urethra and base of the bladder, particularly of the sphincter urethrae membranaceae, which is voluntary. Kennedy showed by experiment with a urethral bag connected with a water manometer that the sphincter around the middle third of the urethra resisted twice as much pressure as did the sphincter around the inner third. By the use of the same technique he found that women with stress incontinence showed without exception a relative weakness of the muscles of the membranous portion of the urethra. He argued that loss of control was due to weakness of the inner and middle sphincter muscles and that restoration of function would follow a reconstructive operation upon this portion of the urethra. The operation is a simple one; briefly, it consists in tightening the urethral muscles and supports by the insertion of three layers of sutures.

In Counsellor's hands and in the hands of many surgeons in Great Britain the operation has given excellent results.

Scope of trial labour

This is a procedure the merits of which are not properly appreciated. In brief, trial labour means labour at full term under surgical conditions and special observation. The method is advocated as a means of dealing with moderate disproportion in primigravidae and only when the other mechanical factors are so favourable as to justify the reasonable expectation of natural delivery without undue risk to mother and child. Of 127 cases which were treated by Hunter or which came under his observation 53·5 per cent of the patients were delivered by the natural forces, 31·5 per cent by forceps and 15 per cent by Caesarean section, whereas of 100 normal patients in whom there was no discernible disproportion 87 per cent were delivered by the natural forces and 13 per cent by forceps. All cases in which the true conjugate exceeded $3\frac{1}{2}$ inches, all deliveries in which the baby weighed less than 6 pounds and all cases in which a previous pregnancy had been carried beyond the seventh month were excluded. It is evident therefore that Hunter's own series showed definite disproportion. There is however much to be said in favour of trial labour for minor degrees of disproportion and for all doubtful cases in which there is a simulation of disproportion but no evidence of it.

In view of his high standards, Hunter's results go far to meet the objections which have been raised against the method. Some of the criticisms are founded on prejudice or ignorance and have no substance in them; others deserve consideration. It is claimed that the psychological effect of a disastrous first labour may be such as to contraindicate any future attempt at delivery at term. The right treatment for such exceptional cases is Caesarean section preceded by a short trial of labour; if the patient will agree to this, her fears will be allayed and very often a Caesarean section will prove to be unnecessary. In Hunter's series the average duration of labour was thirty-one hours, as against the thirty-two hours forty-nine minutes of Peel's series of premature inductions. Foetal mortality may be much higher after premature induction than after trial labour at term.

Other objections are due to misunderstanding of the scope of this form of treatment. The statement that trial labour in domiciliary practice is worrying to the patient, distressing to the relatives, harassing to the nurse and irksome to the practitioner is perfectly true, but the method is wholly unsuited to domiciliary practice: trial labour implies a hospital, special nursing and expert medical attention.

Another criticism is that the associated maternal morbidity is high and that forceps delivery is common and Caesarean section relatively so. This may be true but it merely emphasizes the need for discretion in the choice of method. The treatment of obstructed labour always demands experience and judgment and particularly so in

trial labour because there are no precise indications for its employment and the result depends so much upon the skill of the obstetrician. In the hands of an inexperienced obstetrician the morbidity will be high, but even in the best hands the treatment of labour complicated by disproportion cannot be as simple as that of normal labour and it is unfair to compare the results and the mortality of the two types of case. Increased incidence of instrumental and operative delivery is inescapable in the case of women who are suffering from a mechanical obstacle which renders natural delivery difficult or impossible, but it does not constitute any criticism of the method. Wisely chosen and skilfully carried out, trial labour is calculated to reduce rather than to increase the incidence of Caesarean section. Its adoption implies the postponement of active interference until the natural forces have been given an opportunity of acting and excludes operations which otherwise would be carried out during pregnancy. The general adoption of the lower segment technique has made the onset of the first stage of labour a desirable preliminary to operation and has still further increased the range of trial labour.

Present position in regard to the rhesus factor

As the result of the discovery of the Rh antigen in human erythrocytes and of the suggestion that iso-immunization to this antigen is the cause of many cases of haemolytic disease of the new-born, several investigators have published series of cases in confirmation of the theory (Levine, Burnham, Katzin and Vogel; Boorman, Dodd and Mollison). It has been established that although only 15 per cent of the population are Rh negative, no less than 90 per cent of the mothers of affected children belong to this group—with specific Rh antibodies in their blood in most cases—and that almost 100 per cent of the babies are Rh positive. Three types of haemolytic disease of the new-born (erythroblastosis foetalis) are recognized: hydrops foetalis, icterus gravis neonatorum and anaemia haemolytica neonatorum. Some cases of intra-uterine death of the foetus and still-birth at or near term are associated with Rh antibodies in the mother's blood and therefore belong to the same group of diseases.

At first it seemed probable that the presence or absence of the Rh factor (agglutinogen) was determined by the existence of a single pair of genes, the one dominant R and the other recessive r, 15 per cent of people being purely recessive (homozygous rr) and the remaining 85 per cent either pure dominants (RR) or mixed heterozygous dominants (Rr). Further investigation has shown however that the presence of a single pair of genes cannot explain the observed phenomena. For example, all types of anti-Rh serums did not agglutinate 85 per cent (the Rh positive fraction) of the population equally, but showed variable reactions with such blood. By means of the use and testing of large numbers of different anti-Rh serums it was discovered that at least seven allelomorphic genes are concerned in the determination of the Rh blood group. Thus, although in the great majority of cases anti-Rh serums are produced by Rh negative people, it may sometimes happen that people who are Rh positive by virtue of the possession of one set of genes may produce antibodies to other cells which carry positive genes of a different type and in very rare cases may even react to cells which are Rh negative. Moreover there are no truly recessive genes, for it has been found that anti-Rh negative (rr) serum will agglutinate the cells of heterozygous Rh positive blood (Rr) although it has not any effect on the homozygous RR type. These and similar considerations have a general bearing on the aetiology and treatment of haemolytic disease and particular reference to the subject of blood transfusion.

Mollison's observations (quoted by Gimson) on the longer survival time of transfused Rh negative blood in the circulation of babies who suffer from haemolytic disease have confirmed the clinical experience that the transfusion of this type of blood is not followed by any deepening of the jaundice such as is sometimes seen after the transfusion of unselected (and therefore probably Rh positive) blood. It cannot be over-emphasized that Rh negative blood must be given to all babies who suffer from this disease as soon as the need for transfusion arises and without waiting for the determination of the Rh factor—which must be made in a specialized laboratory—as the risk involved is too great to permit of delay, and in any case the chance that the child will turn out to be Rh negative is remote. It is also essential that women who have given birth to children who suffer from haemolytic disease should themselves receive only Rh negative blood whenever they require transfusion; otherwise severe and even

fatal reactions may follow. It must be remembered too that haemolytic disease rarely manifests itself before the birth of the second—or more commonly the third—Rh positive child unless the production of antibodies has been stimulated by a previous blood transfusion, in which case a first or second child may be affected. Once an affected child has appeared in a family all further Rh positive children are bound to suffer from one or other form of the disease and the outlook therefore depends upon the prospect of the production by the parents of an Rh negative child.

Race and his colleagues^{1, 2} have shown that the father is homozygous Rh positive (RR) in a much larger proportion of cases than would be expected from the known number of this group among the general population. Nevertheless instances do occur in which the father is heterozygous Rr and in these cases there is an equal chance of the next child being Rh negative and therefore unaffected. The identification of the father's group (Rh) may be established by means of anti-r serums or may be inferred from examination of his blood relations, for if either of his parents or one of his children are found to be Rh negative then, according to Mendel's law, he must be heterozygous.

Although it is thus possible to say that the parents can or cannot produce a healthy child it is not possible to forecast the outcome of any given pregnancy; the findings throughout pregnancy have not so far established any connexion between the antibody titre of the mother and the form and severity of the disease in the child.

GYNAECOLOGY

Precocious puberty

Probably most clinicians regard precocious puberty as a pathological state which is induced by ovarian disease and do not realize that in the larger number of cases the condition is essentially constitutional in origin and unassociated with any gross lesion.

Novak reports nine cases, and divides the causes into three groups: (1) neoplastic, (2) cerebral and (3) constitutional.

(1) Tumours of the adrenal gland produce precocious puberty in either sex, more often in the female than in the male, but in the female the precocity is heterosexual in type and is characterized by hirsuties, hypertrophy of the clitoris and, occasionally, excessive muscular development. The effect is virilizing or masculinizing in character. Adrenal gland tumours thus produce a premature but abnormal sex development in the female and not a precocious puberty in the ordinary sense of that term.

Pineal gland tumours produce a similar effect but they are extremely rare in the female—only one out of the 177 cases collected by Simon occurred in this sex.

Ovarian tumours, which arise from the granulosa or the theca cells of the follicle, bring about a form of precocious puberty which is indistinguishable from the natural event except that ovulation is lacking. Their incidence in childhood is rare; apparently up to 1943 only sixteen cases of precocious puberty due to this cause had been published.

(2) The cerebral type of sex precocity is associated with lesions which affect particularly the hypothalamus and the floor of the third ventricle, such as encephalitis, tumours (including tumours of the pineal gland) and hydrocephalus. Weinberger and Grant have collected fifteen cases of tumours of the hypothalamus alone which were associated with this syndrome.

(3) Novak affirms his belief that precocious puberty may be—and in fact usually is—nothing more than the premature but otherwise physiological onset of the normal function. This point, when taken in conjunction with the inaccessibility of many of the lesions cited above and the undoubted risk involved in dealing with them surgically, should warn clinicians against undue haste in having recourse to any form of active interference.

In support of his view Novak describes the nine cases in detail. The ages of the children were 15 months, 2, 2½, 4, 4½, 6½, 7 (2 cases) and 7½ years. The clinical manifestations were indistinguishable from those of normal puberty except in regard to the age of onset. They resemble the type due to granulosa-celled tumours of the ovary, but differ in that ovulation may occur—a feature which emphasizes the physiological nature of the condition and draws attention to the unfortunate possibility of pregnancy. Lima Medina, the Peruvian child who at the age of 5 years and 8 months gave birth to an infant is certainly an example of this type of precocity.

With regard to diagnosis, it is necessary to make a complete general examination and a special investigation of the endocrine and genital systems. Examination under

anaesthesia should be carried out in all cases and if there is any evidence of enlargement of either ovary laparotomy should be undertaken in order to exclude or remove a granulosa-celled tumour. If all these investigations are negative and fail to bring to light the presence of any gross lesion such as tumour, then it is permissible and indeed desirable to regard the case as constitutional in character and congenital or chromosomal in origin.

Novak considers that the underlying factor which normally brings on puberty at the age of 13 is carried by the chromosome and that this time factor may be advanced or retarded by an abnormality of the gene and thus set the female sex mechanism into action at an abnormally early age. In the management of such children (1) special attention must be paid to the psychological aspect of the situation as it affects the child and the mother and (2) the possibility of ovulation and the risk of pregnancy must not be forgotten.

Ovarian tumours

During recent years interest has been centred chiefly on those ovarian tumours which are believed to have their origin in rests of cells set aside in the early stages of the development of the gonad. These include (1) the masculinizing tumour, the arrhenoblastoma; (2) the neuter tumour, the dysgerminoma; (3) the feminizing tumours, the granulosa-celled and theca-celled tumours and the luteinoma.

The present concept of the feminizing tumours is based on Fischel's views on ovarian development which are now widely accepted and envisage the granulosa, theca and stroma cells of the fully formed ovary as all being derived from the primitive mesenchyme cells which form the bulk of the foetal ovary in the early weeks. If this is true it is not surprising that the majority of these tumours have been found to consist of both theca and granulosa cells, although the relative number of each shows considerable variations as indicated by their nomenclature. The thecoma was first described by Loeffler and Priesel in 1932; it used to be considered to be a separate entity but it is now regarded as being intimately related to the granulosa-celled tumour. Indeed it has been possible, by exposing the ovaries of mice to X-rays, to demonstrate the development of the tumours from the stroma cells, and the tumours have been found to be composed of both types of cells as demonstrated by Foot's staining technique.

The mixed tumours are capable of oestrogen production and thus give rise to their characteristic effects—uterine myohyperplasia, menstrual disturbance, post-menopausal bleeding and so forth. It would appear however that the very few reported tumours which can be regarded as pure thecomas have not had feminizing effects. Normal granulosa cells and theca cells are both capable of being luteinized and the same is true of tumours composed of these cells. When this occurs, the tumour becomes a luteinoma (luteoma) and its symptoms are similar to those of the parent tumour. Luteinization of the tumours has also been produced experimentally in animals. Clinically, most of the ovarian neoplasms are innocent or exhibit malignant properties of a very low grade. Occasionally however they occur in a highly malignant form.

Ovarian tumours also arise from cell rests of displaced embryonic tissues, and include the following types.

Brenner tumour.—This is an innocent tumour which often occurs in association with a pseudo-mucinous cystadenoma. It has no special symptomatology but its origin is in dispute. Both Arey and Danforth point out the special appearance of the nucleus in the tumour cells and agree with the majority of writers that the tumour arises from the Walthard islands—a view first propounded by Meyer. The origin of Walthard cells, however, remains in doubt. They may be genetically related to indifferent elements of the male type or may arise from coelomic cells (Arey). In any case Schiller^{1,2} considers the Brenner tumour to arise from Wolffian tissue.

Adrenal-like tumour.—This tumour has also been described as the hypernephroma and the luteinoma. Some of the reported cases have been metastatic growths secondary to a renal hypernephroma (Kannerstein, Brown and Rosen). The majority of the tumours described have not been primary in the ovary (Kleine).

The primary adrenal-like tumour behaves as a rule like an adrenal cortical tumour. It has an androgenic function and has a virilizing or at least a defeminizing effect on the patient. It may give rise to Cushing's syndrome.

Mesonephroma.—This tumour was first described by Schiller in 1939. It is believed to owe its origin to displaced elements of the mesonephros, to which tissue it shows a

close histological resemblance. Some authors prefer to regard it as a papillo-endothelioma. The tumour is rare and does not produce any characteristic symptoms. As a rule it is malignant.

Time of human ovulation

Fresh evidence in regard to the time relation between ovulation and the menstrual cycle has been brought forward by Rock and Hertig, who have published data which are based on a study of eleven fertilized and three unfertilized human ova. The unfertilized ova were obtained by laparotomy and washing out of the tubes. Their cases were submitted to an investigation which included the menstrual history, the histology of the endometrium removed by biopsy, the histology of the follicle and the cytology of the egg.

For example, one specimen was an ovum removed from its unruptured follicle in the ovary on the eleventh day of the cycle of a patient whose previous thirteen recorded cycles had ranged from 25 to 29 days and thus established a mean cycle of 27 ± 2 days. By histological examination and comparison with endometriums the menstrual age of which was known, it was computed that the endometrium had reached a stage of development indicating that menstruation was due in rather more than fourteen days. The histology of the follicle itself disclosed that the connective tissue cells of the theca interna were in a state of distinct luteinization and thus indicated that rupture (ovulation) was imminent. Finally, the cytology of the egg showed an ovum in the process of completion of the first maturation division, that is, on the verge of ovulation.

The eleven fertilized ova were dealt with in a similar manner; the date of ovulation was calculated from the age of the embryo and the histology of the endometrium. The writers' findings support the view that ovulation takes place about fourteen days before the first day of the next menstruation.

PRESENT POSITION OF HORMONE THERAPY AND ITS LIMITATIONS

The results of work done on the development of endocrine therapy in gynaecology and obstetrics have been recorded by Bishop and may be summarized as follows.

Synthetic oestrogens

Stilboestrol has the same biological effect as has oestrone; it is very active when given by the mouth but is liable to cause toxic symptoms if given in large doses (1–5 milligrams). These symptoms have never been recorded in pregnant or puerperal women, but are prone to occur in menopausal cases.

Hexoestrol has a similar action but is less toxic and much less effective—it is one-fifth to one-tenth as potent as is stilboestrol. Another oestrogen, dienoestrol, has been given a limited trial and has been found to be more active and less toxic than is stilboestrol. A fourth synthetic oestrogen which is unrelated to stilboestrol, octofollin (2:4-di(*para*hydroxyphenyl)-3-ethyl hexane), was introduced in 1942; it resembles hexoestrol in its action.

Synthetic progestogen compounds

Ethisterone given by the mouth has a similar effect upon the endometrium to that of progesterone but it is much less active and is capable of producing toxic effects; it is therefore only a moderately effective substitute for progesterone.

Synthetic androgenic compound

Methyl testosterone, a synthetically prepared androgen, when given orally is said to be about one-third as effective as is testosterone propionate given by injection.

Modes of administration

Compared with the parenteral method, oral administration is painless and it has the added advantage of maintaining the hormone at a more constant level in the blood so long as the compound is given in divided doses at regular intervals. Buccal absorption is claimed to be superior to alimentary assimilation and this method has been in use since 1940 in the form of linguets, small tablets which are placed under the tongue or between the lip and gum; nevertheless there is a great wastage of hormone and it is impossible to say how much will be absorbed by the mouth or the bowel. In order to

overcome these several objections the subcutaneous implantation method, whereby a pellet of crystalloid hormone is introduced under the skin, has been tried. It is a most economical method and one which ensures a constant blood hormone level over a long period; 100 milligrams of oestradiol remain active for more than two years. Most preparations are well tolerated by the tissues. Progesterone and testosterone propionate are exceptions; both are extruded through the skin in a few weeks' time.

Scope of oestrogen therapy

Menopausal symptoms and post-menopausal atrophic vaginal changes give the clearest indication for oestrogen therapy; less than 1 milligram daily is all that is necessary in most cases. Larger amounts may be required in order to overcome vaginal atrophy, but overdosage produces mammary discomfort and uterine bleeding and may render the tissues resistant to smaller doses.

Painful engorgement of breasts.—Even in large doses oestrogen will not inhibit lactation if the stimulus of suckling is continued, but it will relieve the pain of engorgement. The initial daily amount should be relatively large (15–20 milligrams) but this dose should be quickly diminished to 5 milligrams or less during the subsequent week or ten days.

Labour.—Oestrogen does not have any effect on the uterus during a normal pregnancy but it will bring on labour in 80 per cent of cases of intra-uterine death with retention of the foetus in utero, when given alone or in conjunction with quinine and pituitary extract. It may be used with success as part of the medicinal induction of labour at or near full term, but it must be given in large doses—up to 20 milligrams hourly for twelve doses. It may also be applied in the treatment of certain types of inertia (so long as there is no element of obstruction) when as much as 50 milligrams should be administered every two hours for five doses.

Scope of progestogen therapy

Functional uterine bleeding.—Results have been disappointing but in cases of endometrial hypertrophy when curettage has failed progesterone may be given a trial; 5-milligram doses may be given daily for ten days during an attack of bleeding and repeated for seven days, commencing nine days before the calculated onset of the next menstrual or bleeding phase; the same dosage may be given for a further period of four days beginning six days before the third period is due.

Threatened and recurrent abortion.—There is good reason to believe that progestogen deficiency is responsible in at least one group of cases and for these women progesterone treatment should be tried. Bishop has adopted the practice of instituting treatment prior to conception; he gives progesterone during the last week of each cycle until a period is missed and administration is continued during the early stages of pregnancy. Dosage should be 5 milligrams daily in the early weeks with even larger doses in later pregnancy if there are signs of uterine activity. The implantation method cannot be applied as progesterone is not tolerated and ethisterone pellets are absorbed too slowly for an adequate level of dosage to be maintained.

Scope of androgen therapy

Functional uterine bleeding.—Androgenic compounds are capable of producing masculinizing effects such as hirsuties and enlargement of the clitoris when given in large doses; care must therefore be exercised in prescribing this hormone. Undesirable effects do not follow the use of moderate doses which are now recognized to be effective in controlling bouts of excessive bleeding and in restoring normal cycles of menstruation. Geist and Salmon observed that up to 300 milligrams of testosterone propionate a month caused immediate relief of excessive bleeding in 91 per cent of cases, without masculinization, and that the effect was lasting in 87 per cent, whereas doses of 500 milligrams or more given early in the cycle inhibited the action of the pituitary gland and led to amenorrhoea and in some cases to masculinization. It is claimed that methyl testosterone given by the mouth has a much less virilizing action than has testosterone propionate given by injection. Berlind found that as much as 3,000 milligrams—equal to 1,000 milligrams of testosterone propionate—could be given monthly without causing any masculinization. In young patients there is a tendency to recurrence but this can be prevented by means of a maintenance dose of 10–20 milligrams administered weekly for some months after the restoration of the normal cycle.

Post-partum breast engorgement and menopausal symptoms.—Androgens may be used for the relief of these conditions but they are less effective than are the oestrogens and are much more costly; they should therefore be reserved for patients who fail to respond to the oestrogens or in whom bleeding begins after their administration. From 10 to 25 milligrams should be given weekly.

Hormone therapy for dysmenorrhoea

Dysmenorrhoea may be due to diverse causes such as disturbance of the autonomic nerve mechanism, ischaemia of the uterine muscle, pelvic congestion and uterine underdevelopment; some of these are amenable to hormone therapy. Oestrogen or androgen therapy affords relief in about half the number of cases; progesterone has not yielded results as good. If oestrogen therapy is chosen, 20,000 international benzoate units of oestradiol benzoate may be given every day for six days beginning on the sixth day of the cycle. When androgens are selected, 20 milligrams of methyl testosterone may be given daily for the ten days preceding the onset of menstruation.

Gonadotrophins and ovulation.—It has been shown that the first substance with gonadotrophic action to be discovered, chorionic gonadotrophin (present in the urine of pregnant women), has not any effect on the human ovary when the substance is given by itself. Serum gonadotrophin (extracted from the blood of pregnant mares and thought to be a pure pituitary secretion) is capable of stimulating ovulation in healthy human ovaries, but has a less certain effect upon ovaries which are insensitive or refractory to pituitary stimulation. Much depends upon the method of administration and the dosage. It has been claimed that the one-two cycle of treatment—serum gonadotrophin followed by chorionic gonadotrophin—gives better results than does serum gonadotrophin alone. It has also been shown that extracts of the pituitary gland contain a factor—Evans's pituitary synergist—which augments the activity of chorionic gonadotrophin but not that of serum gonadotrophin—itself a pituitary derivative—and that together they form a valuable combination.

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ALIMENTARY TRACT DISEASES

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With a section on **LIVER FUNCTION TESTS** by ALICE STEWART, M.D., M.R.C.P.

GASTRIC AND DUODENAL ULCER

More patients are admitted into British hospitals at the present time for gastric and duodenal ulcer than for any other condition. A considerable proportion have been previously treated in hospital for the same condition once, twice or still more frequently. There are two reasons for this unsatisfactory state of affairs: (1) a large number of patients with ulceration are discharged from hospital long before healing has occurred, and (2) the instructions given to them concerning the precautions they must take in order to prevent a recurrence are totally inadequate. Symptoms generally disappear so rapidly with rest in bed and simple dieting that it is too often assumed that the ulcer has healed within two or three weeks and no steps are taken to ascertain whether this is in fact true. The shortage of hospital beds and the little medical interest of cases of ulcer under treatment prompt house officers to get rid of them at the earliest possible moment. The result is that soon after the patient returns to the conditions under which his ulcer originally developed, it becomes active again. If, in contrast with this procedure, he is kept on the strictest treatment until all the evidence points to complete healing, and if he then keeps to a proper 'post-ulcer regime', a new ulcer is unlikely to develop.

The high incidence of gastric and duodenal ulcer will not be materially reduced until every town hospital is provided with a country annexe for the treatment of chronic diseases. A patient with ulcer will then be taken into the central hospital for diagnosis and for the first fortnight of strict treatment, after which he will be transferred to the country to continue treatment in bed for as many weeks as are likely to be necessary for complete healing to occur. At the end of this period he will return to the central hospital for re-examination, and he will then be sent for a final period to the country for more strict treatment if healing is still incomplete. The treatment will in any case end with a fortnight's rehabilitation, during which he gradually returns to full activity and learns the post-ulcer regime which he must observe. If the treatment is sufficiently strict and is continued for a sufficient period, every ulcer, whether gastric or duodenal, will heal, even if it has penetrated the pancreas. The only definite indication for operation, apart from perforation, is organic obstruction.

The strict treatment should consist in mental and physical rest with frequent non-irritating feeds, together with such alkalis as aluminium hydroxide (aludrox) (see Medical Progress (Critical Survey section) 1944, p. 32) or magnesium trisilicate (magsorbent), and atropine in maximal doses if the acidity is high or the pain persistent (see Surveys and Abstracts 1939, p. 46). The strict treatment should be continued without modification until all spontaneous pain and all tenderness and rigidity have disappeared, until there is no occult blood in the stools and until an X-ray examination shows no traces of an ulcer crater. In no case should the treatment last for less than four weeks. Often six or eight weeks are needed in order to secure complete healing, and for large gastric ulcers still longer periods. In the case of gastric ulcers a gastroscopic examination should be made about a fortnight after the last trace of the 'niche' seen under X-ray examination has disappeared, because experience shows that at least this time must elapse before a sound scar replaces the granulations filling the niche.

STRICT ULCER TREATMENT

The patient should remain in bed on the strict treatment without alteration until healing is complete.

Every even hour whilst awake 5 ounces of milk. This may be warm or cold and may be flavoured with tea.

Every odd hour a 5-ounce feed, which may be made of any of the following:

(1) Arrowroot, farola, Benger's food, Horlick's malted milk, junket, custard. These may be made

more appetizing by the addition of a little jelly (red currant, apple or other fruit) and the junket may be flavoured with chocolate.

(2) At least two should consist of a thick soup or semi-solid *purée* of potato, artichoke, cauliflower or parsnip.

During the night the patient should have citrated milk by his bedside, so that whenever he wakes he can take a feed.

A rusk, plain biscuit or thin bread with butter or honey may be eaten with any of the feeds. A 'coddled' egg may be taken once or twice a day.

Small quantities of water may be drunk between feeds. An ounce of strained tomato or of strained orange or other fruit juice should be taken with three of the drinks. When these are unobtainable, 100 milligrams of ascorbic acid dissolved in milk should be given daily.

Ten grains of sodium citrate in a teaspoonful of water should be added to each milk feed.

A drachm of atropine mixture ($\frac{1}{10}$ grain of atropine sulphate in 1 drachm of water) is given before the last feed and before two or three other feeds if the acidity is high. The dose should be increased by 10 minims every day until an unpleasant degree of dryness of the mouth or paralysis of accommodation occurs; the dose should then be reduced to that of the previous day.

Half a teaspoonful of aludrox or of magsorbent may be given with a little water half-way between feeds and a teaspoonful last thing at night.

Wash the mouth out after each feed.

No smoking during the strict treatment.

NOTES

(1) Strict treatment should be continued without any alteration until there is (a) no spontaneous pain, (b) no tenderness or rigidity, (c) no occult blood in three consecutive stools, (d) no 'niche' to be seen under X-ray examination, and (e), in case of gastric ulcer, no ulcer to be seen with the gastroscope. Test (c) should not be made until (a) and (b) are negative and (d) not until (c) is negative. In no case should strict treatment last for less than four weeks; generally from six to eight weeks and sometimes much longer are required.

(2) In gastric ulcer and in duodenal ulcer with mild symptoms, two-hourly feeds suffice. In other duodenal ulcer cases, especially with high acidity, and in all cases in which pain persists for more than three days, hourly feeds are essential.

(3) If there is any gastric stasis, no feeds after 7 p.m.; evacuate completely at 10 p.m. until no more than 5 ounces are present on three consecutive nights.

(4) If nocturnal pain continues give a continuous milk 'drip' into the stomach through a tube during the night.

(5) If all discomfort disappears within 48 hours, it is unnecessary to give atropine, aludrox or magsorbent.

Chronic and recurrent ulceration

Chronic gastric ulcer is the result of long-continued irritation of the stomach in people with a gastric ulcer diathesis. The irritation may be mechanical or chemical. The chief mechanical irritants are food which has been insufficiently chewed as the result of hurrying over meals, deficient teeth or badly fitting dentures, and food which is coarse or badly cooked. The chief chemical irritants are condiments, alcohol taken on an empty stomach, and swallowed tobacco juice. A quite different type of stomach—the characteristic features of which are hyperchlorhydria and rapid evacuation—predisposes to duodenal ulcer. It is futile to give a patient with an ulcer a period of strict treatment, if steps are not taken to prevent the recurrence of the ulcer when he returns to work after it has healed by giving him a regime which he must follow for the rest of his life. It should be explained to him that his recent illness is the result of a constitutional tendency and that a recurrence is almost certain if he returns to the conditions of life which preceded its onset. However long he remains free from symptoms he must keep to the new regime, as he will never outgrow the constitutional tendency which is as much a part of himself as is his external appearance. I tell such patients that if they ever have a recurrence it will certainly be either their fault or mine—theirs if they have not kept to the rules, mine if they have. If it is my fault, I shall have to give them a better planned regime, but I can tell them beforehand that the chances are at least ten to one that it will prove to be their fault, not mine.

Post-ulcer treatment

I have drawn up a post-ulcer regime, which has been revised from time to time during the last twenty-five years and especially recently in order to fit in with war-time conditions. It differs materially from most regimes which are given to patients who leave hospital after a period of strict treatment for ulcer or after operations for ulcer, in that comparatively little attention is paid to details about what they may and may not eat compared with those concerning how and when they should eat; attention too is drawn to other important factors, such as fatigue, anxiety, infections and tobacco. It is of course essential to discuss the regime in detail with each individual patient and to modify it when necessary in the light of his own past experience as regards the factors

which have preceded the onset of the attacks of active ulceration. It is also important to remember that whereas extrinsic factors are of special importance in gastric ulcer, psychological factors are generally of chief importance in duodenal and anastomotic ulcers. In hospital the regime should be explained by the physician or his house officer, and not by the dietician, whose interest is likely to be concentrated on the relatively unimportant details of diet. It is also much better to tell a patient what he should avoid than to give him standard meals which are often quite impossible for him to obtain.

It is quite easy to arrange for the two-hourly feeds in almost every civil occupation with the help of the two pints of milk at present allowed to 'ulcer patients' and the occasional addition of their sweet ration in the form of plain chocolate and of biscuits when they are obtainable. A lorry driver, farm labourer, or clerk can take the milk with him in a bottle and have a drink as often as is necessary, so that it does not matter if (in the case of the lorry driver, for example) dinner is taken at irregular hours and long periods elapse between proper meals.

The note about aspirin (10) is of special importance if a patient has had a haemorrhage, as it is not only the most common cause of haematemesis in the absence of other gastric symptoms, but is also occasionally the cause of haemorrhage in patients with a chronic ulcer.

POST-ULCER REGIME

(to be followed permanently)

(1) A meal or feed (milk, plain biscuit or plain chocolate) should be taken at intervals of not more than two hours from waking to retiring, and again whenever you wake during the night.

(2) Eat slowly and chew very thoroughly. Adequate time should be allowed for meals, which must be punctual. Avoid taking a meal when you are tired; first rest for at least a quarter of an hour. When there is not time for a proper meal, it is better to drink some milk or eat some plain chocolate or biscuits than to bolt some less digestible solid food.

(3) Do not smoke more than six cigarettes or two pipes a day; they should be smoked after meals. Cigarettes should have an absorbent plug in the mouthpiece. Do not smoke at all if you have any indigestion.

(4) During periods of overwork, and especially of mental stress, whenever possible one day or half-day a week should be spent resting in bed or on a couch, or lying out of doors, on a strict hourly or two-hourly diet, even in the complete absence of digestive symptoms. If you are much worried or are sleeping badly, ask your doctor for a sedative.

(5) Special care should be taken to avoid chills. If you get a cold, sore throat, influenza or other infection, remain in bed on a very light diet until you have completely recovered.

(6) Avoid alcohol, except (if desired) a small quantity of beer, light wine or diluted whisky taken with (but never before) meals. Avoid pips and skins of fruit (raw, cooked or in jam) and raisins, currants, figs, ginger and lemon-peel in puddings and cakes, nuts and unripe fruit. Avoid radishes and raw celery, tomato skins, stringy French beans, hard peas and beans. Coarse green vegetables (cabbage etc.) must be passed through a fine sieve.

Avoid porridge made with coarse oatmeal, and wholemeal and similar biscuits, tough meat, mustard, pepper, vinegar, curry, pickles and chutney.

If in doubt about any food, remember that you must not eat anything which cannot be chewed into a mush.

(7) A teaspoonful of aludrox or magsorbent should be taken an hour after meals and also whenever the slightest indigestion or heartburn is felt.

(8) Liquid paraffin may be taken for the bowels, if necessary, but no other aperient should be used.

(9) Visit your dentist regularly every six months.

(10) Take no drugs in pill or tablet form. Take no aspirin or any tablet containing aspirin. If needed, powdered calcium aspirin can be taken with water instead of aspirin.

(11) If you have the slightest return of symptoms, go to bed on a strict diet at once. Consult your doctor and do not wait for the symptoms to become serious.

LIVER FUNCTION TESTS

A recent article by Higgins, O'Brien, Stewart and Witts, entitled 'A Clinical Evaluation of some Tests of Liver Function', is welcome because, although it is not a comprehensive review, it is a serious attempt to compare the merits and demerits of a number of tests in ordinary hospital practice. The writers chose their tests to cover a wide range of liver functions—estimations for the plasma bilirubin, phosphatase, albumin and globulin and hippuric acid and laevulose tolerance tests. They obtained values for each test in (1) one hundred healthy individuals, (2) in seventy-two patients with proved disease of the liver and (3) in sixty-three patients with other diseases. Having done this, the writers were able to show that all the tests were acceptable as liver function tests, because they gave values in cases of established liver disease which were significantly different from those obtained in the other two groups. This did not necessarily prove however that the tests were of any clinical value, and a further

analysis of the results in the liver disease group showed that in practice not all were worth making.

Comparative data in liver disorders

In twenty-two cases of acute hepatitis the severity of the attack was accurately reflected in the height of the serum bilirubin, but the other tests added nothing to the clinical knowledge. In nineteen cases, in which jaundice recurred or persisted for over two months, the serum bilirubin was no longer a reliable guide to prognosis. The patients who eventually died or who were left with chronic liver damage were best distinguished from those who recovered by the characteristic changes in the plasma albumin and globulin. A fall in the plasma albumin occurred in the early weeks of acute hepatitis but normal values were rapidly restored as recovery went forward; in the two patients who died the changes were not significantly different from those which were found in the milder cases. In eight fatal cases there was a much more dramatic fall in the plasma albumin accompanied by a rise in the plasma globulin; in two cases the latter eventually became four times as high as the former. In five patients in whom chronic liver damage developed there was a persistent although less striking reversal of the albumin ratio. In six patients who eventually recovered completely the protein changes were like those found in the cases of acute hepatitis. In fourteen patients with chronic hepatitis, who had never had a recognizable acute or subacute episode and showed little or no jaundice, the plasma protein findings were similar to those found in the five cases in which the disease went through a subacute phase and eventually became chronic.

Although in the acute, subacute and chronic cases the hippuric acid test and plasma phosphatase test often gave valuable supporting evidence of liver damage, they were not sufficiently reliable as individual tests of prognosis. The laevulose index was a better indication of the degree of liver damage but the test was regarded as inconvenient in clinical practice because it involved repeated venepuncture.

In nine cases of intense jaundice due to extrahepatic obstruction there was a moderate fall in the plasma albumin but little or no rise in the globulin. The most characteristic finding in addition to the high bilirubinaemia was a remarkable rise in the plasma phosphatase. This had not been observed in the severely jaundiced cases of acute hepatitis.

In the sixty-three patients with other diseases there were often deviations from the normal in single tests but never consistent changes in the series as a whole.

The article referred to has been quoted at some length because, although it deals with only a few recognized liver function tests, it shows one way in which such tests can be evaluated. It draws attention to the fallacy of regarding any test which gives abnormal results in the presence of liver damage as necessarily of value in clinical practice and to the danger of relying on the results from a single test to decide whether or not a patient has liver damage.

Comparative evaluation of liver tests

The following tentative conclusions have been drawn from this and other recent publications on liver function tests.

Serum bilirubin test.—The fact that jaundice is so easy to detect should not lead one to underestimate the value of a quantitative measurement of the serum bilirubin. This gives an accurate indication of what can be only roughly gauged by the eye, and is the best method we have of judging the effect of any therapeutic agent in acute hepatitis. The test is simple to perform and is to be preferred to the qualitative van den Bergh reactions which are apt to be misleading if interpreted too literally.

Plasma protein test.—In cases of persistent jaundice there is sometimes uncertainty whether they are of the obstructive or of the hepatic type, and there is often doubt whether or not the liver has suffered irreparable damage. Any test must be valuable which may prevent an unnecessary laparotomy—an operation which is fraught with danger in cases of hepatitis—and may indicate the prognosis. If in addition the test can be made on a single sample of venous blood, which can be used for other estimations, it is to be preferred to more elaborate tests for routine use. The tests which appear to fulfil these conditions best are those which give an accurate measurement of the plasma proteins. In order to obtain reliable results an accurate method based on the micro-Kjeldahl estimation of nitrogen should be used. This requires the assistance

of an experienced biochemist and of a well equipped laboratory. Other methods of protein analysis, such as the biuret method, which are much simpler to perform, may give unreliable results.

Flocculation tests.—Flocculation tests, such as the Takata-Ara, the colloidal gold and the cephalin flocculation, are qualitative tests dependent upon changes in the plasma proteins. At present they have a much more limited value than the quantitative methods have. Recently electrophoretic methods have been described which are capable of detecting very delicate changes in the arrangement of the plasma proteins, but they have as yet no place in the ordinary clinical laboratory.

Excretion of dye and hippuric acid tests.—Several tests which depend upon the excretion of dye-stuffs, such as santonin, bromsulphalein and rose bengal, have been described. There is not, however, any good evidence that either these or the hippuric acid test can make it possible to distinguish between temporary disturbance of liver function and permanent damage. Serial records indicate the general trend of the illness but they do not anticipate clinical judgment as does the estimation of the plasma proteins. Such tests may provide valuable supporting evidence of liver damage, and they are useful if there is reason to suspect that unusual plasma protein findings are due to other diseases.

Laevulose tolerance test.—The laevulose tolerance test is an index of the part played by the liver in carbohydrate metabolism. This function is often only moderately affected in acute hepatitis whereas in chronic liver diseases it is usually grossly impaired. It is however an inconvenient test as it cannot be made if there is much vomiting, and it involves several venepunctures.

Plasma phosphatase test.—The plasma phosphatase is liable to alteration in several diseases and the test should not be used alone as an indication of liver damage. Jaundice with a high plasma phosphatase and relatively little disturbance of the albumin-globulin ratio is more likely to be due to extrahepatic obstruction than to hepatitis.

Plasma cholesterol test.—There are wide variations in the level of the plasma cholesterol in health and no characteristic changes in liver diseases.

Combination of tests.—In order to arrive at the decision whether or not a disease is accompanied by liver damage, it is useless to rely on results obtained from a single test. The abnormal plasma protein findings in myelomatosis provide an illustration of the kind of fallacy which may result from insufficient evidence. In this disease the other liver function tests would give normal data.

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ANAESTHESIA AND ANALGESIA

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The following review of the progress which has been made in the field of anaesthesia and analgesia covers only the period which began with the outbreak of the present war. When the arduous conditions in which the majority of British anaesthetists have existed are considered, it is remarkable to be able to record so many advances in this special subject.

PREMEDICATION

The current tendency is to use comparatively light premedication—often with morphine and scopolamine (hyoscine)—and then to induce anaesthesia with intravenous pentothal sodium.

Intravenous morphine

It has been found in air-raid and front line practice that if morphine is given hypodermically to a cold and shocked patient, absorption is very slow on account of the impaired circulation. Because he still complains of pain a second dose may be administered and then as resuscitative measures begin to take effect the circulation improves and symptoms of morphine poisoning may occur. Many essential operations have had to be postponed until this condition had been adequately treated. If a small initial dose of morphine is given intravenously its full effect develops within a few minutes and the difficulty does not arise.

Basal narcosis

If it is considered desirable for the patient to be rendered completely unconscious in bed, rectally administered paraldehyde or bromethol is generally used.

INHALATION ANAESTHESIA AND ANALGESIA

Ether vaporizers

Although diethyl ether has many obvious disadvantages it is still used extensively for inhalation anaesthesia, usually as an adjuvant to nitrous oxide and oxygen. Owing to the lack of apparatus or the absence of a skilled anaesthetist, ether must sometimes be used alone and several new vaporizers have been devised since the beginning of the present war.

The Oxford Vaporizer No. 1 is the most ambitious and has been used with success in the North African and in other campaigns. It works on the 'draw-over' principle, that is to say the patient inspires air through the apparatus and in transit ether vapour of variable and known concentration is added (Macintosh and Mendelssohn). The addition is accomplished by means of a lever which diverts any desired proportion of the inspired air through an ether chamber the temperature of which is kept constant by means of a chemical thermostat. A concertina type of Connell bellows enables artificial respiration to be carried out if necessary. The Oxford vaporizer is probably the best and most accurate means of administering ether and air. The difficulties of inducing anaesthesia have been minimized in the later models by the provision of a small rebreathing bag near the face-piece into which ethyl chloride or divinyl ether may be sprayed (Bannister). The nuisance and danger of contaminating the surrounding atmosphere by large quantities of ether vapour from the expiratory valve are at present receiving attention and it is possible that the adsorption of ether by means of activated charcoal may prove to be satisfactory (Epstein). The chief disadvantages of the Oxford vaporizer are its bulk and its weight and the necessity of having a supply of hot water for the purpose of keeping the temperature of the water jacket within the prescribed limits.

A simpler and lighter apparatus which works on the same draw-over principle has been devised for ether, for trichlorethylene or for both drugs simultaneously (Marrett).

Trichlorethylene

The only new anaesthetic drug to attain any popularity is trichlorethylene, which has the formula $\text{CHCl}:\text{CCl}_2$. It is a heavy liquid (specific gravity 1.47) with a characteristic non-pungent smell and with a boiling point of about 88°C . and a vapour density of 4.53. It is not inflammable and its vapour will not explode when mixed with any proportion of air. At high temperatures however oxygen-trichlorethylene mixtures may be inflammable. For anaesthetic purposes, purified trichlorethylene is stabilized by the addition of 0.01 per cent thymol. One variety is coloured blue and is sold under the name, trilene (Hewer^{1,2}).

Owing to its low volatility, trilene is not suitable for an open mask administration but it can be used in a simple vaporizer such as Marrett's inhaler or it can be added as an adjuvant to nitrous oxide and oxygen. It should not, however, be used in a closed circuit (Humphrey and McClelland) as under certain conditions it may be decomposed by hot soda-lime into dichloroacetylene, which is toxic and may cause nerve palsies (Carden).

Trilene vapour is not irritant to the respiratory passages, and a rapid and pleasant induction of anaesthesia is usually possible. The blood pressure is generally within normal limits and cut surfaces do not ooze unduly. Cardiac irregularities are fairly common, as is the case when cyclopropane is used, and are usually of the nature of auricular extrasystoles. Muscular relaxation may be difficult to attain, in which case a change-over to ether is desirable, as deep narcosis with trichlorethylene may be accompanied by rapid and gasping respiration. The analgesic properties of the drug are remarkable and they have been turned to account in dentistry (Hill) and in midwifery (Freedman). During prolonged anaesthesia the maintenance dose of trilene is very small indeed and administration should be suspended some time before the end of operation. Neglect of this precaution may lead to delayed recovery.

Closed circuit technique

The increasing popularity of cyclopropane is partly responsible for the general swing-over from partial to total rebreathing. Apart altogether from expensive gases such as cyclopropane it is really absurd to use much the greater part of the narcotic agent to keep the carbon dioxide percentage at a reasonable level and the residue for the purpose of anaesthetizing the patient. Economy in gases is desirable in peace but it is essential in war (Hewer³). The closed circuit technique has enabled severely wounded soldiers to have the benefits of a gas anaesthesia although they may be many hundreds of miles away from their base. Experiences in the North African campaign have shown that cyclopropane anaesthesia is perfectly feasible even near the front line of a rapidly advancing army.

Although economy is the most obvious advantage of the closed circuit method, there is no doubt that the technique is more in line with physiological processes than is partial rebreathing: respiration is not continually stimulated by excess of carbon dioxide and, since the respired gases are saturated and at body temperature, there is much less heat and fluid lost through respiration. The fact that no anaesthetic vapours escape into the atmosphere contributes to the freshness of the operating team and to a lessened risk of explosion if inflammable vapours are used.

The to-and-fro system has the merits of simplicity and efficiency but some of the war-time soda-lime is dusty and becomes extremely hot. The patient's tissues may therefore become congested; he may perspire and may inhale irritating alkaline particles. For these reasons the circle system is gradually becoming more popular. In one recent model leaks are virtually eliminated by the use of one casting for the absorber; at the same time careful design has reduced the resistance to respiration to the negligible figure of from two to four millimetres of water (Mushin).

Controlled respiration

This practice has come to the fore in anaesthesia only during the past few years, and under certain conditions may prove to be of much value. The first stage in the technique is to abolish natural respiration; this can be accomplished in one of three ways as follows. (1) By depressing the respiratory centre by means of drugs so that it will

no longer respond to the normal carbon dioxide stimulus. (2) By lowering the carbon dioxide tension in the blood by means of hyperventilation while the patient breathes through a carbon dioxide absorber so that there is insufficient carbon dioxide to stimulate the respiratory centre. (3) By the use of a combination of both methods (Nosworthy^{1, 2}).

On reflection it will be seen that the first technique is indistinguishable from anaesthetic overdosage, and it should be avoided. The second is physiologically sound but may be technically difficult to achieve especially when narcotics which in moderate dosage tend to stimulate respiration are used. In practice therefore the third or combined technique is generally used, often with cyclopropane as the anaesthetic agent.

When natural respiration has ceased, the respiratory exchange is carried on by means of rhythmic compression of the rebreathing bag of the closed circuit apparatus. Certain modern machines such as Mushin's absorber are specially designed with a rebreathing bag of bellows type which is fitted with a lever so that compression is facilitated.

Controlled respiration is particularly useful for the repair of thoraco-abdominal wounds and in cases of diaphragmatic hernia, in which the temporary absence of any respiratory movements may make all the difference to the surgeon when he is suturing the diaphragm and adjacent structures. The method has certain pitfalls and should not be attempted by the inexperienced anaesthetist.

INTRAVENOUS ANAESTHESIA

Pentothal sodium

Of the many barbiturates with an action of short duration which have been introduced during the past few years, pentothal sodium has proved to be the most generally satisfactory. Owing to its irritant action on the tissues the 10 per cent solution has now been abandoned and a 5 per cent concentration is being used for most purposes.

Indications.—Many patients dislike the feel of a face-piece, a difficulty which is overcome by intravenous induction. It is unfortunate that general practitioners have acquired the habit of promising patients that they will be put to sleep in bed. This practice certainly increases the anaesthetic risk since, if severe spasm or collapse should occur, the anaesthetist has no means of coping with it and may be separated from his apparatus in the operating theatre by long passages and lifts.

Apart from their use in the induction of anaesthesia the intravenous barbiturates have proved to be of very great value during the present war for all types of work in the front line and elsewhere in which inhalation narcosis is difficult to obtain. A surprising amount can be done with a 20-cubic centimetre syringe by adding minimal doses from time to time as they are required. For long operations the addition of repeated doses of pentothal to a continuous drip saline is preferable to a continuous drip of the diluted drug from a single bottle; countless more or less home-made contrivances to achieve this end have been described by anaesthetists in the Forces.

Contra-indications.—Apart from the recognized contra-indications such as respiratory obstruction and suppurations in and around the mouth, it is essential that pentothal be given by an experienced anaesthetist. An example of the dangers which beset the indiscriminate use of the method was provided after the Japanese air-raid on Pearl Harbour in December 1941 (Halford).

INTRAVENOUS ANALGESIA

Intravenous local analgesia

This was introduced by Bier in 1909 and had some vogue for operations on limbs. For example, to produce analgesia in an adult arm about 10 cubic centimetres of a 2 per cent procaine hydrochloride (novocain) solution was injected intravenously with a tourniquet in position in the course of thirty-five minutes. This method has now fallen into disuse.

Intravenous general analgesia

This appears to offer a hopeful field for research. It has been shown that a slow drip infusion of 0.2 per cent procaine hydrochloride in from 5 to 10 per cent glucose relieves the intense pruritus of jaundice and provides sufficient analgesia for painful burn dressings. The period of infusion is from one to one and a half hours and the quantity used is from 60 to 500 cubic centimetres. It is said that relief from pain lasts for from two to twelve hours (Gordon).

LOCAL ANALGESIA

In Great Britain local analgesia alone is almost confined to minor surgery as the average citizen greatly prefers to be unconscious not only during a major operation but for some time before and after it. During the past few years however anaesthetists have extended and developed many local techniques which they employ in combination with light general narcosis; the latter may be maintained either by inhalation or by the intravenous route.

The drug most commonly employed for infiltration is still procaine hydrochloride, usually as a 0.5 per cent solution combined with 1 in 250,000 adrenaline. If a prolonged effect is required, the use of amethocaine hydrochloride (decicain, pantocaine) has grown in popularity recently, the usual concentration being 1 in 1,000 (James¹).

For very prolonged analgesia the fractional or repeated dose technique has been developed. For example, fractional caudal block has been used with success in obstetrics. A malleable needle is introduced into the sacral hiatus and repeated doses of the analgesic solution can be given from a continuous flow syringe connected with the needle by rubber tubing (Hingson and Edwards).

The time consumed in performing extensive infiltrations can be materially diminished by the use of mechanical infiltrators. A most efficient machine has been developed recently; it is basically a modified spray gun in which the pistol grip terminates in a needle mount. Pressure is supplied by means of either a carbon dioxide cylinder or a motor tyre pump (James²).

Refrigeration local analgesia

An ethyl chloride spray has been used for many years for the purpose of freezing small areas of skin and thus of making them insensitive to an incision.

The method has been developed recently for amputations in shocked patients and in those who are bad risks. The site of the tourniquet is first determined and the limb is packed round with ice bags at this point. After some time it will be found that the tourniquet can be applied painlessly. Crushed ice in rubber sheeting is then wrapped round the limb or it may be immersed in a pail of ice water for from one and a half to two and a half hours. The tissue temperature will fall to between 5° C. and 15° C., and amputation can be carried out painlessly. It is said that pain and shock are often diminished but there is no doubt unfortunately that delay in healing occurs (Allen).

SPINAL ANALGESIA

The term spinal analgesia covers two separate methods of simultaneous blocking of spinal nerves by a single injection.

Extradural spinal block (epidural analgesia)

Analgesic fluid can be deposited at any level of the peridural space, the needle being inserted between two spinous processes. The point of the needle must not enter the dural sac and until recently there was no means of being certain that the correct position had been reached. It has now been shown that there is a negative pressure in the peridural space and by the use of the 'hanging drop' technique or of a special indicator the chances of error are greatly reduced (Odom). Extradural spinal block has not however made much progress in Great Britain.

Subarachnoid spinal block

This is the usual method of spinal analgesia. By it a solution of the analgesic drug is mixed with the cerebrospinal fluid through lumbar puncture carried out not higher than from the second to the third lumbar interspace. For low block, heavy (hyperbaric) solutions of procaine hydrochloride or of amylocaine hydrochloride (stovaine) are usually employed. The lumbar puncture is made with the patient either sitting up or in the lateral position with the affected side downwards. Heavy nupercaine may be used if a prolonged analgesia is required.

High block, for example for gastric surgery, is as a rule carried out with light (hypobaric) nupercaine either by the original technique described by Howard Jones or by Norman Lake's modification thereof. The advantage of the use of a light solution for high block is that any degree of head-down tilt may be used at once to mitigate a fall in blood pressure without risk of an excessive spread upwards of paralysis.

The cause of the pressure fall is still the subject of much argument; one of the recent theories is that it is a paralysis of the adrenal glands with consequent hyposecretion

of adrenaline (Pitkin). The logical treatment would thus seem to be the employment of continuous intravenous infusion of adrenaline and this practice has been carried out with success by the use of a dilution of 1 in 250,000 (Evans).

Fractional spinal analgesia has been used in an attempt to obtain a prolonged analgesia with some controllability. The original technique was to insert a malleable lumbar puncture needle connected to a syringe by rubber tubing and to inject repeated doses as required. The projecting part of the needle lay in the gap of a slotted sorbo-rubber mattress (Chivers). One of the drawbacks to this method is the risk of broken needles, and various modifications of the technique have been tried although none has become standardized. It cannot be said that fractional spinal block has been adopted with much enthusiasm in Great Britain but the method may have possibilities.

CHARTS AND RECORDS

For some time past anaesthetists have kept blood pressure and pulse rate charts during severe operations in order to keep an accurate check on the patient's condition and to observe the onset of shock or other abnormal signs. In recent years efforts have been made to improve these charts, so that not only should detailed records of anaesthetics be available for subsequent study, but also any required information be forthcoming without laborious hand sorting.

In the United States of America the Hollerith punch card system was modified for anaesthetic records (Chivers) and is now used fairly extensively in spite of the drawbacks of an arbitrary code and the need for a mechanical sorting machine (Wangeman). In Great Britain a simpler type of combined chart and record has been devised and is being adopted by many Army and civil hospitals (Nosworthy³). All round the edges of the card are perforations each of which has a certain 'positive factor' printed against it. During operation the anaesthetist rings round each relevant positive factor in ink or with a sharp pencil. Some days after operation the cards are completed and at any subsequent time the encircled holes are converted by the use of scissors into U-shaped slots. The extraction of any desired information can be made with great ease by inserting a knitting needle into the required positive factor hole and lifting it upwards. All the cards which have had this hole converted into a slot will remain in the pack which can be again sorted for additional information. This system is not only proving its worth in estimation of the value of new techniques but is extremely useful for the teaching of students.

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ACUTE INFECTIVE DISEASES

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It has been complacently accepted, often without adequate examination of the facts, that the health of the country has withstood well the strains and risks of war and has passed through the worst phase unscathed. Little can be gathered from the epidemiological data of a single year because even in times of peace favourable and unfavourable phases are encountered each year and over longer periods according to seasonal and secular fluctuations, some of which are peculiar to a particular disease or group of diseases whereas others are common to the majority of epidemic diseases. The war-time epidemiological pattern is more evident when the yearly figures are compared with the average for the three immediately preceding years in respect of incidence and mortality. The year 1943 presents a balance-sheet in which the gains are almost completely offset by the losses. Scarlet fever, diphtheria, measles, whooping-cough and the enteric fevers have declined in mortality and (scarlet fever excepted) perhaps also in incidence; exact figures for measles and whooping-cough are not, however, available before 1939 in which year these diseases were made generally notifiable. On the other hand, the war has witnessed an increase in cerebrospinal fever, acute pneumonia, influenza, dysentery, and diarrhoeal diseases in the young, all of which have tended to become more deadly. The notifications given below apply to England and Wales and the deaths to the 126 great towns.

		AVERAGE, 1937-9	1940	1941	1942	1943
Diphtheria	-	58,500	46,683	51,091	42,318	35,944
Deaths -	-	1,472	1,409	1,530	987	759
Scarlet fever	-	91,158	65,573	69,111	84,932	116,217
Deaths -	-	149	80	58	55	69
Measles	-	..	407,908	406,507	285,300	374,198
Deaths -	-	624	485	503	293	397
Whooping-cough	-	..	53,403	171,406	65,563	95,859
Deaths -	-	801	356	1,205	468	605
Typhoid fever and Paratyphoid fever	-	1,176	2,824	4,703	887	707
Deaths -	-	85	56	79	38	26
Dysentery	-	3,413	2,843	6,597	7,177	7,772
Cerebrospinal fever	-	1,319	12,791	11,119	6,089	3,380
Acute pneumonia	-	47,736	47,712	50,514	42,487	52,225
Influenza	-
Deaths -	-	4,899	5,510	2,993	1,544	6,280
Diarrhoea and Enteritis under 2 years of age	-
Deaths -	-	2,164	1,812	1,947	2,283	2,569

The downward trend of diphtheria is positive if not dramatic and invites more vigorous action rather than complacency in immunization campaigns. The number of confirmed cases of diphtheria is known to be much less; it sometimes approaches one half the number of notifications, the percentage error in diagnosis rising despite improved bacteriological facilities; these improvements are in fact a major cause of the rise, since carriers, even of negligible numbers of organisms, tend to be included. The behaviour of cerebrospinal fever is seen to imitate closely that during the war of 1914-18 although at a higher level, but the death rate has been kept low owing to the

life-saving virtues of chemotherapy. Dysentery—a relatively trivial disease in Great Britain—and infective enteritis in infants—still a deadly disorder—continue to give cause for anxiety, as do other infective diseases such as influenza, tuberculosis and the venereal diseases; social, environmental and economic factors, some of which are directly related to the war effort, such as increased use of processed foods and inadequate food storage accommodation in the home and occasionally in communal catering establishments, play their part too. As far as infant morbidity is concerned premature weaning, increasing illegitimacy and, from the infective standpoint, badly planned and inadequately staffed day and residential nurseries, must be looked on as having an adverse effect.

The influence of social conditions on four important infective diseases in children in London since 1924 was studied in considerable detail by Wright and Wright. Correlation co-efficients were found to indicate a connexion between the extent of sub-standard housing conditions in the different boroughs and the mortality of young children from each of four specified diseases: the association was closest with measles and less close in decreasing order with whooping-cough, tuberculosis (all forms) and diphtheria. Significant correlations also emerged between both the social index and the index number below the poverty line and the mortality from each disease; in respect of diphtheria alone there was a positive correlation between mortality and the mean number of children in each family. The impact of war on tuberculosis was studied by Stocks and Lewis-Faning, who found that the relation between notifications and deaths no longer gave as reliable an index of incidence as it had given in the years before the present war; it was calculated that 2,900 persons suffering from notifiable diseases died during 1940–1 who normally would have survived until 1943, and during the period 1940–3 there were 6,000 more deaths from respiratory tuberculosis than would have been expected in years of peace.

The threat of a serious epidemic of influenza appeared to be imminent at one time during the year, but did not materialize, although certain conditions were favourable. At the beginning of 1943 localized outbreaks of virus B influenza were encountered but the disease remained mild and failed to establish itself in epidemic form; in the spring and summer virus A influenza made its appearance but also failed to attain epidemic proportions. It reappeared in November, rather more than two months earlier than the expected time; this portended a severe and widespread epidemic but the looked-for danger signal—the predilection for subjects under thirty years of age which was a noteworthy feature in the 1918–19 pandemic—was not observed. Although attacks were generally mild the mortality was the highest since 1933; as compared with conditions which existed during the war of 1914–18, the more favourable nutritional and environmental circumstances of the present-war period probably constitute the crucial difference, but the influenza enigma is too complex for more than a tentative conclusion to be drawn.

INFECTION, RE-INFECTION AND CROSS INFECTION

Preventive measures in hospital

Interest in the epidemiological and clinical problems of infections acquired in hospital and in the measures for their elimination has remained unabated although the early faith in some of the measures advocated has had to be modified if not abandoned. The aerosols have generally proved to be impracticable in use. Ultra-violet irradiation has a few enthusiastic sponsors in America, chiefly in the field of the prevention of virus infections (notably chicken-pox and measles) but bacteria are vulnerable to it only if they are assailed before they acquire a protective covering of dust. The elimination of dust is the most practicable line of attack but the methods used so far, for example oiling of floors and blankets, have not proved to be an unqualified success. In a recent investigation Wright, Cruickshank and Gunn showed that the treatment of floors alone failed to reduce atmospheric pollution as estimated by numbers of living organisms determined by the slit sampler, but that oiling of all fabrics, personal linen and room furnishings, combined with floor treatment, was effective. The practical difficulties in the way of providing a steady laundry service able to cope with the technical requirements are considerable, particularly in war-time, but need not be insurmountable. The occasional appearance in patients with exanthemata of dermatitis from either the oil or the fixing agent is a positive contra-indication to its use in the nursing of subjects with sensitive skins; friction appears to be a major factor in the

production of dermatitis since patch tests have proved to be uniformly negative. The subject of the prevention of cross infection in its diverse aspects, together with practical rules and methods, is incorporated in a special Medical Research Council memorandum. The need for individual isolation of infectious or potentially infectious children, for constant vigilance in observance of the rules of aseptic nursing technique (including proper use of gowns and masks) and for prompt exclusion of all persons proved or suspected to harbour pathogenic organisms, is stressed; it is conceded, however, that considerable structural alterations and additions to equipment and staff are required in order to enable a satisfactory standard to be attained and maintained. The use of air conditioning and of fabrics which do not harbour dust may provide a solution to some of the outstanding problems.

Treatment of carriers

Another approach to the question of infection was made more recently by myself (publication pending). I tried to ascertain the conditions which favoured continuance of the carrier condition, and used various antibiotic agents in order to kill or to inhibit pathogens or to prevent them from leaving their hosts. The use in the past of chemicals in the form of gargles, douches, sprays and insufflations, although universally recommended and tried, has not shown itself to be effective or to be free from the risk of trauma to mucous membranes since these are generally more vulnerable than are the organisms which invade them. The sulphonamides, which have an inhibitory rather than a bactericidal action, tend to be removed from the buccal cavity by secretions and friction too rapidly to be effective, whereas systemic administration is uncertain in its action—with rare exceptions such as that on the feebly viable meningococci. Among a large number of tested preparations, I found that a powder consisting of sulphanilamide, sulphathiazole and aspirin in equal proportions by weight adhered well for from one to two hours by virtue of the last named, which also quickly relieved local pain, but that speedy elimination of organisms was not effected. Penicillin (5,000 units per cubic centimetre) and patulin (1 in 1,000 dilution) were employed for acute infections and carrier conditions—chiefly haemolytic streptococci and diphtheria organisms—in the throat, nose and middle ear, generally with favourable and occasionally with dramatic results. Among a number of inorganic substances tried the best was 2 : 7-diaminoacridine hydrochloride, an acridine compound allied to proflavine but more active and less toxic (Ungar and Robinson) which in 1 in 1,000 dilution gave comparable and in some respects better results especially against penicillin-resistant organisms such as coliform bacilli, *Bacillus proteus* and *Bacillus pyocyaneus*. Patulin exhibited a wider inhibitory range but was relatively poor against haemolytic streptococci and diphtheria organisms, as compared with penicillin; the risk in higher concentrations of damage to epithelial cells led to the final abandonment of patulin. Organisms deeply entrenched in the crypts of chronically diseased tonsils tended to defy every effort to dislodge them but once the tonsils and adenoids had been dealt with rapid elimination was the rule. Should these methods and substances prove to be widely applicable the elaborate techniques at present recommended in the prevention of infection and of cross infection would become superfluous.

ADVANCES IN DIAGNOSIS AND IN TECHNICAL METHODS OF INVESTIGATION

Measles

The successful cultivation of the virus of measles on the chorio-allantoic membrane of the growing chick embryo and the production of immunity by vaccination with egg-passage attenuated virus, as evidenced by resistance to further vaccination or to natural attack, give cause for hope that these cultural methods or a serological test of immunity will at an early date facilitate routine diagnosis in respect of measles.

Whooping-cough

The early diagnosis of whooping-cough has been expedited by cultivation of *Bacillus pertussis* from a nasopharyngeal swab on a special Bordet medium treated with dilute penicillin, which inhibits most inhabitants of the human respiratory mucosa but leaves pertussis organisms unaffected (Cruickshank). Although the percentage of positives is not materially greater than it is on the routine cough plate, the fact that the swab can be taken at any time—so that there is no need to wait for (and possibly miss) a paroxysm—greatly enhances its practical value to the busy practitioner.

Diphtheria

The exact diagnosis of diphtheria has been more difficult since an appreciable proportion of the population has been immunized (Neubauer) as there is a tendency to take a swab in every instance of sore throat. In doubtful cases the Schick test, followed by antitoxin administration six hours later is recommended, or better still, removal of a sample of blood for antitoxic titre and antitoxin administration immediately thereafter, especially if the patient has been immunized. The result should answer the question whether or not the patient has tonsillitis and is at the same time a carrier of diphtheria organisms—a not uncommon finding amongst fever hospital staffs. Experience has shown that gravis and intermediate strains are almost invariably virulent and to an approximately equal extent, whereas some 10–15 per cent of mitis strains are avirulent; this makes the animal test always worth while.

Glandular fever

Exudative or ulcerative tonsillitis in adults not infrequently fails to show any of the usual pathogens on culture. A full blood count and a Paul-Bunnell test usually reveal the nature of the disease, which is more prevalent and pleomorphic than is generally realized. Halcrow, Owen and Rodger have described a hospital outbreak of infective mononucleosis with some unusual features; of 290 cases (patients and nursing and medical staffs) in which evidence of the disease was manifested by blood examination and the Paul-Bunnell reaction, in 125 only was clinical evidence of the disease observed. There was not any response to sulphonamides, which is the usual experience, but there does not appear to be any particular risk in giving them.

Gingivitis

The part played by nutrition deficiency, particularly avitaminosis, in the production of or predisposition to morbid conditions in the mouth has been investigated by King, Francklyn and Allen, who found in refugees from Gibraltar who were compared with London school children of similar age, a high incidence of gingivitis which appeared to respond to the giving of nicotinic acid and to a less extent to administration of yeast (*Torula utilis*). The absence of fever and other constitutional disturbance differentiates this condition from the form of gingivo-stomatitis which is caused by the virus of herpes simplex described by Scott and Steigman, but does not exclude the possibility of an infective as opposed to an entirely nutritional aetiology.

Enteric and dysenteric infections

It is probable that the recently recorded increase of dysenteric infections was largely artificial, due partly to the employment of selective media (desoxycholate-citrate-agar) and partly to increased appreciation of the influence of even trivial diarrhoeal attacks and of contact carriers in the spread of the disease. The Sonne form is still the prevailing type and it is generally resistant to sulphonamides. Typhoid fever outbreaks are nowadays rare and when they occur are limited; the increasing mobility of the civil population and of members of the Forces often makes detection of the source of infection difficult but the Vi antibody test and phage-typing of organisms constitute reliable aids, as was shown recently by Felix and by Bradley. Some light has been shed upon the aetiology of neonatal gastro-enteritis by the experiments of Light and Hodes who reproduced in young calves a clinically similar disease by means of the nasal instillation of filtered stools from infants affected in institutional outbreaks. As it is difficult to prevent some of the material from being swallowed the route of infection may have been intestinal. Infected calves were found to be immune against subsequent vaccination and a few experiments suggested that a specific antibody had developed in the serums of some at least of the sick babies.

Atypical and influenzal pneumonia

The increasing percentage of cases of atypical pneumonia, as compared with the classical pneumococcal disease, and the lack of response to sulphonamides have stimulated the search for a filter-passing agent similar to the psittacosis virus which has a known special affinity for lung tissue. In a recent case described by Perrone and Wright which responded at least temporarily to blood transfusion fatal meningo-encephalitis ensued, with neurological changes allied rather to those characteristic of epidemic

than of post-infective encephalitis. Animal inoculations of lung and brain tissues gave a negative reaction except in one rabbit which died of an encephalitozoon infection after brain tissue inoculation. Some of the cases labelled atypical pneumonia are doubtless instances of sporadic influenzal pneumonia although perhaps on the whole influenza is diagnosed more often than the facts warrant. Difficulties of isolation of the influenza virus during inter-epidemic periods and during minor outbreaks have been experienced by Stuart-Harris, Glover and Mills; virus B appears to be particularly elusive whether in experimental animals or on chick embryo and strains hitherto undiscovered or unidentified may well be responsible for some of the so-called atypical pneumonias which are encountered.

SULPHONAMIDES AND PENICILLIN IN THE TREATMENT OF FEVERS

Sulphonamides

The continued search for new sulphonamide compounds provides sufficient evidence that the perfect chemotherapeutic agent has yet to be discovered. As long as considerations of supply and cost operate it is not possible to establish whether or not sulphadiazine is, as most American workers claim, the best all-round preparation for systemic use if not for local application. Although the immediate toxicity of sulphadiazine is low, granulocytopenia occurs as often with its use as it does with the use of other preparations, and by reason of its low solubility the tendency to cause renal damage is greater. Increasing experience of sulphamezathine (sulphadimethylpyrimidine) has proved it to be as effective as is sulphadiazine when judged by the case mortality amongst a comparable series; the effects of both compared favourably with those of the more toxic sulphapyridine (Morgan and Wylie-Smith). The low toxicity and high solubility of sulphamezathine make it particularly suitable for babies with parenteral diarrhoea, especially since a soluble salt has been available for intravenous or medullary administration. In America sulphamerazine (a substance similar to sulphamezathine) and sulphadiazine have been tried concurrently in two groups. Geffer, Rose, Domm and Flippin found sulphamerazine (sulphamethylpyrimidine) to be readily absorbed and slowly excreted with consequent maintenance of a high blood concentration, with moderate dosage; it was comparable to sulphadiazine in toxicity and in therapeutic activity against pneumonia and cerebrospinal fever. With regard to therapeutic efficiency, absence of side-effects and avoidance of induction of drug resistance, the superiority of a short intensive course over a prolonged low dosage is now generally appreciated, but the use of excessive doses, such as those recently recorded by Smith, of the so-called intestinal sulphonamides—notably sulphaguanidine—is hardly ever justified. For dysentery Smith gave 142 grammes of sulphaguanidine to forty-four female adults over a period of ten days; about the ninth day in no fewer than twenty-one patients various toxic rashes developed—scarlatiniform, morbilliform, urticarial and petechial—associated in some instances with severe constitutional disturbances; eight out of twelve patients reacted to a test dose of the compound but not to other sulphonamides, which indicated that the guanidine radical was the sensitizing agent. Even more heroic doses although for a shorter period were given to three soldiers in the Middle East, in whom developed acute confusional psychoses characterized by disorientation, semi-stupor and in one case by catatonia with respiration of the Cheyne-Stokes type; all recovered after the drug was stopped and they appeared to suffer no permanent harm (Crofton and Diggle). Other workers have found sulphapyridine, sulphathiazole and sulphasuxidine (succinylsulphathiazole) to be as effective as sulphaguanidine but the recorded series are too small to provide evidence for a decisive verdict.

Penicillin

The risks and uncertainties of chemotherapy contributed to the enthusiastic reception which was given to penicillin. The substance however suffers from serious disadvantages: it is unstable in solution; it must be given parenterally; it has to be given often (every two or four hours) and the administration tends to be painful; like the sulphonamides, in ordinary doses it is merely bacteriostatic in action and therefore prolonged treatment is sometimes necessary; finally it is scarce and is expensive to produce. The chemical constitution of penicillin is unknown and blood concentrations cannot be determined except by the crude method of inhibiting known sensitive

organisms in culture. Perhaps its action is most remarkable against staphylococcal infections (although some 4 per cent of strains are resistant) but it is also active against a wide range of organisms including those of diphtheria—notable exceptions are the organisms *Bacillus tuberculosis*, *Bacillus pertussis*, *Bacillus coli*, *Bacillus proteus* and *Bacillus pyocyaneus*. My own experience (unpublished) of the drug has been favourable in streptococcal and staphylococcal septicaemia but not in anaerobic streptococcal blood infections. Against septic meningitis its efficacy appears to depend directly upon success in applying it to the affected parts (Fleming); the presence of fibrinopurulent adhesions may render this difficult or even impossible.

Patulin

Another mould product, patulin, has shown an even wider bacteriostatic and bactericidal activity, including in its range the coliform bacilli, *B. proteus* and *B. pyocyaneus*, but it is toxic to tissues and is safe only in high dilution on mucous membranes. Probably the favourable results recorded in respect of the common cold were attributable to the inhibitory effect on the bacterial flora of the respiratory tract and not to the direct virucidal activity. The encouraging findings amongst men of the Navy which were reported by Raistrick, Birkinshaw, Michael, Bracken, Gye, Hopkins and Greenwood, were not confirmed by experience of its use in the Army (War Office Report, 1943). A large-scale trial of the substance is being carried out under Medical Research Council auspices among industrial workers, with the declared aim of assessing finally its efficacy against colds.

RECENT ADVANCES IN PROPHYLAXIS

Typhoid fever and paratyphoid fever

The British Army authorities in 1944 decided to change over from the well known efficient heat-killed T.A.B. vaccine preserved in carbol-saline to a new preparation killed by 75 per cent and preserved in 25 per cent alcohol; this vaccine, T.A.B. alc., contains the full complement of Vi antigen in stable form upon which immunity production depends. Other advantages are fewer and less severe general and local reactions, although an initial stinging pain is the rule. The dose has been reduced: for men it is now 0.25 cubic centimetre with 0.5 cubic centimetre given at least fourteen days later; for women it is 0.2 cubic centimetre and 0.4 cubic centimetre respectively; an annual re-inoculation of 0.25 cubic centimetre is recommended for both sexes (Army Medical Department Bulletin).

Bacillary dysentery

A new vaccine against bacillary dysentery of the Shiga type has been prepared by Morgan and Schütze who gave two inoculations of a phenol-extracted O antigen of *Bacillus shigae*, with an interval of six weeks between them, to twelve adult volunteers; in all specific agglutinins developed which rose from less than 1 in 6 in each instance to an average of 1 in 30, that is by 500 per cent; this compares favourably with the rise in Vi and O agglutinins after antityphoid inoculations.

Whooping-cough

A combined alum precipitated pertussis vaccine and diphtheria toxoid was used by Kendrick in a series of 1,326 cases of children of school age and the results were compared with two earlier series in which plain pertussis vaccine was used and with an uninoculated control group otherwise similar in all material respects. On the basis of known subsequent exposure to whooping-cough the disease developed in 20 per cent of the inoculated and in 87.2 per cent of the uninoculated; comparison with the earlier vaccine was not unfavourable. Combination of antigens simplifies administrative work, and spares children the discomfort of numerous injections. An alum precipitated pertussis vaccine (Glaxo) is available in Great Britain and is at present on trial; three injections of 0.5 cubic centimetre (total dosage 30,000 million organisms) at four-weekly intervals are recommended to be given at the age of six months and onwards, and 1 cubic centimetre should be repeated at two-yearly intervals. No reactions have been encountered other than the local discomfort and an occasional tender nodule at the injection site, similar to that seen with diphtheria toxoid.

Influenza

The experience of active immunization by subcutaneous injection against influenza, whether the antigen is used alone or is combined with mixed vaccines of respiratory pathogens, has been on the whole disappointing. In order to imitate the natural process more closely Burnet employed intranasal administration of three strains of virus (two A and one B) attenuated by egg passage. Symptoms after vaccination were generally trivial but some patients had coryza with or without malaise and headache. The best antibody responses were obtained in those who had low initial titres but there was not any association between the responses to A and to B viruses. In an epidemic of influenza in one Army unit of about 7,000 men previously vaccinated it was found that at most only minor benefit accrued from the immunization. Similar methods of vaccination against measles have been employed by Stokes and Rake and their associates; they found that an inhaled spray was the most efficient route of administration since it returned 98 per cent positive measles reactions as against 80 per cent after intradermal inoculations and 30 per cent after intranasal drip. In the latest report Rake claimed to have immunized without untoward effect 1,281 children presumed to be susceptible; subsequent observation of about two-thirds of the total number disclosed that 450 (54 per cent) showed positive evidence of modified disease; on the basis of results shown in a small group of forty-six vaccinated children who were intimately exposed—of whom six had unmodified attacks, twelve had modified attacks and the remaining twenty-eight escaped—he concluded that a further trial of the prophylaxis was warranted.

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MENTAL DISEASES

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To speak of physiology, biochemistry, electrophysics and the like as sciences ancillary to psychiatry is perhaps to insult these disciplines. The term, fundamental, is becoming a more and more watertight description of their relation to the systematized body of clinical knowledge which we call psychiatry. To say this is not to imply that in their terms we are near to a satisfactory description of the aberrations of human feeling and conduct; but we are perhaps nearer that goal in certain abnormal mental states than we are in describing normal human conduct. Few psychiatric problems however are likely to find a satisfactory formulation in physiological terms so long as the essence of purposiveness in Nature eludes us and non-material values actuate mankind.

RESEARCH IN FUNDAMENTAL SCIENCES

Research in fundamental sciences in the sense described has naturally been restricted by the present war. There have recently appeared, however, some books and monographs which summarize much work done in the preceding years. Gellhorn's *Autonomic Regulations* includes some observations on the physiology of shock treatment in mental disorders. He concludes that all such methods have one effect in common—stimulation of the vagus-insulin and of the sympathetic-adrenal systems, especially the latter—and he suggests that it is by these means that they become effective, at least in schizophrenic conditions.

The application of Pavlovian concepts to the problem of mental disorder has been studied by Masserman, who has enlarged the mechanical Pavlovian approach by taking into account the instinctive drives that lie behind all disorders of the organism as a whole. To read Pavlov's work one would imagine that the organism was nothing but a bundle of mechanical reflexes. This restricted attitude is abandoned by Masserman, who adapts Pavlovian technique to the study of conflict of motives such as those arising from hunger and fear instead of confining himself to a consideration, say, of the effects of attempting to differentiate sounds of various frequencies. He established in his experiments with cats the following results.

(1) The conflict set up produced what he designated 'chronic anxiety', manifested by restlessness, trembling, crouching, hiding, 'startle' responses to minor sensory stimuli and recurrent or chronic disturbances of pulse and respiration.

(2) 'Phobic' responses, symbolic of the stimulation which produced the emotional conflict, for example instead of welcoming the feeding signal the animal would develop the above symptoms and would attempt to escape. Some animals starved themselves although food was easily accessible and in others compulsive behaviour developed. These manifestations could be cured by rest, reassurance (hand feeding and petting), forced solution (when the animal was pushed towards the food box), 'social imitation' by placing near the feeding box a normal animal, which promptly ate without inhibition, and by 'working through', that is, by persistence in spite of the exhibition of the frightening stimulus. How close these analogies are to human psychoneurotic reactions and what they mean, is naturally a matter for discussion. No one can deny that the analogies are striking. Animal experiments on the function of the hypothalamus have indicated that the latter may integrate and possibly reinforce the affective neural impulses which control some of the sympathetic and motor manifestations of fear and of rage, but there is little or no evidence that the hypothalamus governs or even mediates the emotional experiences themselves (Masserman).

The above experimental result has to be taken in conjunction with clinical observation of the effects on the emotional life of lesions of the hypothalamus (Wyburn-Mason). Masserman emphasizes that 'an emotion is a highly integrated, conative and affective somatic reaction in which not only the central nervous system but the entire

organism is concerned'. Philosophical considerations cause us to add that the entire organism is more than the sum of its parts.

With regard to the partial mechanisms of emotional expression, it has been claimed recently that if the blood of patients who display anxiety and fear is added to Ringer-Tyrode solution in which a strip of rabbit intestine is suspended, the rhythmic contractions of the latter are altered in a manner which resembles the effect of cholinergic drugs (Milhorat, Small, Doty and Bartels). Some evidence has been presented recently that in the blood of all patients in the manic phase of manic-depressive psychoses also there is a substance which has a sympathicomimetic—in this case an adrenal—effect. It has been found that adrenalectomized cats which received the blood of manic patients by intraperitoneal injection were able to survive for a considerably longer time than those which received blood from a normal person.

In the margin between the clinical and the experimental fields of investigation Wolff has shown that the human gastric mucosa is in life very much affected by emotional changes. He has studied a man aged fifty-seven years with a permanent surgical gastric fistula. Anxiety, hostility and resentment produced acceleration of acid secretion, hypermotility and hyperaemia. When this state was prolonged, the mucosa showed unusual susceptibility to injury and the pain threshold was lowered so that otherwise painless contractions, acid concentrations and mechanical stimuli became painful. Moreover, if the protection of the usual coating of mucus was absent even minor trauma caused erosions and haemorrhages and, when the acid gastric juice encountered a surface so denuded, peptic ulcer was apt to result (Wolff; Wolf and Wolff).

How much can still be done in a purely clinical field and how much of fundamental importance remains to be explored in a scientific manner is well illustrated by a paper by Slater¹ in which, in a statistical analysis of two thousand cases mainly of psychoneurotic types of reaction, are described six main syndromes, namely obsessional, hysterical, paranoid, anxious, depressive and hypochondriac. The statistical analysis indicated that 'of all neurotic symptoms, obsessional symptoms are most firmly rooted in a basis of specific predisposition, the next in order being hysterical and paranoid symptomatology. Depressive and anxious symptoms are distinctly less closely related to the endogenous predisposition, and hypochondriasis, at least as here defined, least of all.'

Although constitutional disposition cannot be anywhere entirely excluded Slater does allow that a neurosis may be set up on the basis of individual experience. The oft-quoted similarity of some of the phenomena of battle neurosis to conditioned reflexes suggests to him, as to others, that 'conditioning' in childhood may have analogous effects in producing neurotic response in adult life. Slater points out that the distinction between 'psychopathic personality' and 'psychoneurosis' is unscientific and that it is a mere convention that reactions which take an aggressive form tend to be called psychopathic, whereas anxiety and instability of mood and the like are called psychoneurotic. Psychopathic personality he regards simply as an extreme form of the neurotic constitution. It has been pointed out elsewhere that some psychopathic personalities may fall in the series of constitutional types and others in the series of reaction types (Gillespie).

Such difficulties illustrate the need for a collaboration of the investigator interested in dynamic psychopathology with the worker who approaches the problem from a formal and statistical point of view. The former would not have much hesitation in regarding some psychopathic personalities as essentially psychoneurotic in structure (the result of individual experience in the formation of complexes) whereas others he would regard as dependent almost entirely upon inborn constitution.

Slater remarks on the impoverished sex life of many of the defectives and psychopaths; this has been observed also in many psychoneurotics. Clinical experience suggests that, contrary to the vulgar belief, such persons are usually not neurotic because of an inhibited sex life but have an inadequate sexual urge as the result of the same constitutional and other factors that make them neurotic.

With regard to the oft-debated question of the existence of a real difference between endogenous depressions and reactive depressions, Slater concludes that 'the question can be put to a specific test which yields a decisive result' in favour of a real difference. The question never was a purely academic one, since it is always important to know when to apply psychotherapy of the less superficial kind and when to withhold it; but the introduction of electrical convulsion treatment, which suits endogenous de-

pressions better than it does reactive ones and has little or no effect on psychoneurotic anxiety states except to make them worse, has brought a new urgency to the problem. Slater concludes that the best general indications of the neurotic constitution are found in abnormal personality, neurosis in childhood, positive family history and poor work record.

It is surprising to find so good an exponent of statistical methods in psychiatry as Slater quoting the opinion which Curran expressed about patients in civil life, that the results of simple out-patient supervision are as good as are those claimed by the exponents of intensive psychotherapy, since in the 'follow-up' upon which this opinion was based the author succeeded in tracing only 40 per cent of the original cases and no one can say what happened to the others.

What has already been said of the significance of the label of psychopathic personality in some cases is supported by a study of forty such individuals who were detained for periods up to one year in institutions. In a considerable proportion of them it was found that the family pattern was that of an aggressive father, interested only in success, and a doting weak mother; hence a spoiled-child attitude to life emerged in the adolescent, coupled with a tendency which might or might not be unconscious to avenge himself on the father by delinquent acts which in some cases seemed like adult versions of temper tantrums. That these assumptions and the treatment based on them were valid is suggested by the result. Sixteen (40 per cent) were said to have remained stable after discharge up to the time of reporting. This seems an unusually good result for the treatment of psychopathic personalities (Heaver). All such discussions however are handicapped by the vagueness of the concepts of 'psychopathic personality' and 'neurotic constitution'.

TREATMENT OF MENTAL DISEASE

Electrical convulsion therapy

This has established itself as the method of choice in involuntional melancholia. In depressions at the earlier ages it is almost equally successful (Batt¹). Kalinowsky and Worthing claim that the results in schizophrenia are equal to those obtained with insulin provided that the treatment is adequate, which in their opinion means at least twenty, and possibly more, convulsions. Eight treatments are judged to be adequate in depressions and often as many as this are not necessary. Small voltages producing *petit mal* are ineffective and might be actually harmful (Ziskind). Kennedy claims to have treated successfully by the same method obsessional hand-washing, obsessional jealousy and obsessional number-counting with paranoid delusions. He believes that these are symptomatic of a manic-depressive constitution.

The most recent histopathological evidence is to the effect that convulsion therapy produces only reversible brain damage (Bowman; Barrera). Sodium amytal, a dose of 300 milligrams intravenously, has been given before convulsion therapy is applied, primarily for the purpose of soothing apprehensive patients and of preventing fractures; it is also helpful in the management of post-convulsive excitements, although, in lessening the severity of the fit, it makes more fits necessary. Other advantages claimed for it are that it is useful for eliciting prognostic data beforehand and that the electroencephalogram returns to the normal more quickly afterwards (Impastato, Bak, Frosch and Wortis).

Insulin treatment

There is still some doubt about the exact effectiveness to be assigned to insulin in the treatment of schizophrenia. About its immediate effects there is not any doubt. It can change the symptom picture and shorten the illness. How much difference it makes in the long run is more difficult to ascertain. It is claimed that the ultimate recovery rate is superior to that obtained by any other method and that the quality of the result is better; there are however many relapses and it is a constantly recurring experience in later observation of the results that the percentage of recoveries or improvements diminishes as time advances. Those who have set out to investigate the problem have unfortunately been hampered by statistical and other difficulties. Thus Rennie lumps together insulin coma and convulsion therapy as 'shock therapy'. In a 'follow-up' of 500 cases including both affective and schizophrenic psychoses which had been treated by these methods, he finds that the results in affective psychoses are much better than those in schizophrenias, whereas in schizophrenias they are no

better—in fact they are worse—than those in a control group; he does, however, include a fair proportion of cases of admittedly poor prognosis in the insulin-treated group. The best controlled experiment so far appears to be that by Gottlieb and Huston, who compared the results in sixty-six insulin-treated cases with those in 142 controls of closely similar age and clinical type. They could not find any difference in the end-result but they point out that in their insulin treatments they did not increase the dose beyond that directly necessary to produce coma.

Bond and Rivers had previously reported a comparison between eighty-two patients who had been treated according to these principles and seventy-two who had been treated by increasing the dosage so as to produce longer and deeper stupor; convulsions were not regarded as a contra-indication. By the former method 34 per cent had recovered twelve months after treatment compared with 57 per cent by the latter method, but twelve months is not a sufficiently reliable period for a 'follow-up' of this kind and the authors do not give any details which would enable anyone to judge how comparable the groups were in their clinical and other features.

The current answer to criticism of the ultimate efficiency of insulin coma treatment is that it is efficacious but depends mainly upon the skill of the doctor who gives it. This is a reasonable answer but at present it has the status of an opinion only.

In the meantime it is puzzling to observe that Penrose, by the use of statistical methods in an investigation two years later of the results in 196 cases which had been treated by insulin, found that whereas at the end of one year results were better, at the end of two years in the same group the results were actually worse in the insulin-treated than expectation based on pre-insulin experience.

It has been well said that the use of insulin must be combined with all other facilities, re-educational, psychological and so forth (Tennent). As regards the comparison of insulin with electrical convulsion therapy in schizophrenia, the latter method is generally thought to be inferior (Cook).

Treatment of alcoholism

The conditioned reflex treatment of alcoholism continues to increase in popularity, although its employment suggests a desperate abandonment of methods based on experience in favour of one for which only a basis of speculative analogy can be claimed. Alcohol is used as a conditioned stimulus and an emetic as an unconditioned stimulus. Emetine is now more favoured than apomorphine. The mixture prescribed by Voegtlin and Lemere is 50 grains of emetine hydrochloride, 25 grains of pilocarpine nitrate and 23 grains of ephedrine hydrochloride in 40 cubic centimetres of water; an injection is made intramuscularly 4–12 minutes before alcoholic drink is given to the patient.

In so far as the results seem to depend largely upon careful selection of patients and as only a very willing patient is likely to cooperate in such an unpleasant form of treatment, it is doubtful whether any better results are to be expected from this method than from any other. It would be a pity if a mechanical approach of this kind were used irrespective of the nature of the aetiological factors and of the other therapeutic possibilities.

In the United States of America where, unlike Great Britain, the incidence of alcoholic psychosis had been rising between the war of 1914–18 and the present war (Bowman, Solomon and Wortis) a movement called 'Alcoholics Anonymous' has been apparently very useful in reclaiming victims of alcoholic addiction. It is a group movement with a strong ethical bias. The effect of contact with it is said to consist in a loss of aggressiveness, of suspicion and of selfishness (Tiebout). This implies a drastic change in the attitude of the alcoholic who, according to Tiebout, is often narcissistic and egocentric, with feelings of omnipotence. It is certainly the case that alcoholics usually tend to resent advice and to spend much of their time in repeated futile endeavours to prove to everyone that they can drink with impunity. The Alcoholics Anonymous movement seems to be effective in the same way that religious conversion (of the kind fostered for example by the Salvation Army in Great Britain) has often been successful in producing total abstinence.

PSYCHOSOMATIC MEDICINE

Alexander recalls the need for a distinction between the physical symptom which is a conversion phenomenon (that is to say a symbolic substitute for an unbearable idea)

and one which is the direct expression of emotional tension (that is to say a normal physiological event). The only thing which makes such an emotional expression morbid is its chronicity, resulting for example from an unresolved conflict. Alexander maintains that in the various psychosomatic disorders of this sort the relation between the type of underlying motive and its bodily expression is specific. For example, he believes that the 'gastric neurotic' unconsciously chooses gastric symptoms because he wants to be loved and cared for, and the stomach symptoms are a physiological correlate of the instinctive love of food. It appears therefore that even in this physiological type of disturbance Alexander sees a symbolic component. This formulation however is not universally supported by experience so far nor by the studies which have been published regarding the psychological characteristics of individuals with different kinds of psychosomatic ailments such as asthma, high blood pressure and duodenal ulcer. Such individuals tend, according to various studies, to display a recurring pattern of the same type of general personality. It has been several times observed that emotional stress precedes the onset of rheumatoid arthritis (Halliday). I have seen an arthritis flare up suddenly after exposure to bombing. If these are not coincidences, then the question of the physiological processes involved is of interest. It has been observed that emotional stress reduces skin temperature and it is also known that capillary flow is diminished in arthritis. An attempt has therefore been made to determine whether or not emotional factors produce significant peripheral vasomotor factors in arthritis, as judged by skin temperature recorded by means of a Hardy radiometer. The results have been inconclusive; the only general observation made was that skin temperature returned more slowly to the normal in arthritis after mental stress.

Anorexia nervosa is usually considered to be primarily a psychiatric problem, but the menstrual disturbance in this condition has often been considered as secondary to the emotional disturbance or, alternatively, as secondary to the self-starvation promoted by the emotional disturbance. The history however may show that menstruation stopped before the intake of food had been reduced for any length of time and that, even after nutrition has been restored to the normal, menstruation may not reappear for several years. Aub suggests that the essential thing is 'a brittle mechanism of internal secretions', holding that the cessation of menstruation is secondary to impairment of nutrition; unlike other women on a reduced diet, anorexia nervosa patients stop menstruating within six weeks and their excretion of female sex hormones is soon back at a six-year age level, where it remains for three or four years.

The effect of muscular disabilities on the personality has been studied by Ripley, Bohnengel and Milhorat. Such conditions as anterior poliomyelitis have little effect on the mentality of children but the effect becomes apparent with sexual and social maturity. There is anxiety if the onset is sudden; later, compensatory trends are developed, such as self-consciousness and aggressiveness. Some patients become irritable and the irritability is mixed with resentment and jealousy; in some a kind of protective euphoria develops as a cover to an underlying depression, whereas if the disability is severe, apathy is liable to ensue. Subjective improvement tends to follow each trial of a new remedy and this may account for some of the successes claimed for vitamin therapy, the use of glutamic acid and so forth.

OBSERVATIONS ON OTHER CONDITIONS

Child psychiatry

Depression and anxiety with obsessive-compulsive symptoms after respiratory infection have been described. This picture is not uncommon after prolonged physical and emotional stress in adults of obsessional personality. What is interesting in these children is that the picture, as in adults, is that of an obsessional temperament; but whereas the same kind of temperament in adults is rarely modifiable, in the twelve children studied by Richter the results of psychological treatment were striking. From being timid, cowed by authority, perfectionist and meticulous, they became for a time boisterous and pugnacious as the result of the release of hostile and aggressive feelings which had originally been provoked and repressed as the result of jealousy or of conflicts arising from sibling rivalry and so forth.

Prognosis of depressions

The further history of 111 cases of depression in out-patients has been investigated

by Ziegler and Herrsema; of the eighty-four patients who were traced twenty-five had died, seven of them from suicide; this is a high suicide rate and such an end was more common in the recurrent cases. Forty of the fifty-nine known to be alive were working to some extent; four had come to be regarded as schizophrenic. Neurotic and hypochondriacal symptoms suggested chronicity.

Prognostic factors in involutional psychoses have been investigated by Drobnes. In the improved group patients with depressive symptoms had preponderated, whereas in the unimproved group those with apparently schizophrenic symptoms, such as hallucinations and delusions, had been predominant. The suggestion is made that involutional melancholia is either a late manic-depressive state or a schizophrenic one occurring late in life. It is notable that in the unimproved cases the end-result of the originally hallucinated and deluded types was a paranoid dementia, whereas in the group in which depressive symptoms originally preponderated the end-result in the unimproved cases was described as a 'neurasthenic' state. Although these tentative conclusions are based on only fifty-one cases in all, they are in accord with the observation of Brockhausen (Slater²) on the relatives of 201 patients with involutional melancholia. Patients with recurrent attacks were excluded; the remainder were divided into those with and those without a well marked paranoid colouring to the psychosis. Those with the paranoid colouring had a high incidence of schizophrenic psychosis among their relatives; but the non-paranoid group were on the total evidence not manic-depressive in nature. It looks as if involutional melancholia, like schizophrenia, contained hitherto undifferentiated groups of syndromes with different biological foundations.

Mental after-effects of head injury

The mental after-effects of head injury have been investigated from a new point of view by Ruesch, who made repeated examinations at intervals after the injury, using the principle that any inferiority of earlier performances after injury as compared with later ones must indicate the effect of brain damage on mental function. The result seemed to show that the effect of head injury was to produce (1) a defect in judgment, as tested for example by means of 'pictorial absurdities' and 'hole-in-the-board' tests; (2) loss of mental speed, as measured by the ability to name colours and by the use of a tachistoscope and (3) by inability to keep up a sustained effort such as subtraction of serial sevens. Ruesch did not find what is seen in degenerative brain disease such as occurs in senility, namely diminution in capacity for forming abstractions, in retention, and in the estimation of spatial relationships. This observation seems to conflict with previous experience of severe brain injuries in which the capacity for abstraction has been found (for example by Goldstein) to be permanently impaired after an interval of time. Ruesch found that the impairment in cases of severe head injury was no worse than the impairment after milder damage. His observation that his cases did not improve after three months is not in accord with other clinical experience, in which improvement in mental capacity has been noted to be continuous up to as long as two years after the original injury.

Geriatrics

The sharp increase in the rate of first admissions to mental hospitals of patients with psychoses in later life (Page and Landis), and general considerations as well, have caused a number of psychiatrists to turn their attention to the organic psychoses of old age. They point out that the prognosis in such cases, especially in those of arteriosclerosis, is much better than it is generally supposed to be (Palmer, Braceland and Hastings). The methods of treatment employed were the removal of infection and the cure of constipation, provision of high caloric and high vitamin diet, increase of fluid intake, rest, adoption of a routine of occupation and exercise in suitable proportions and simple psychotherapy. They advocate the administration of 5 per cent glucose per rectum—a method considered by some to be useless since the glucose is probably not absorbed.

Prefrontal leucotomy

This may now be considered to be well established as a therapeutic measure. Provided that the cases are chosen with discrimination the results can be dramatic, especially in some very agitated impulsive chronic schizophrenics. Cases of intractable depression with obsessional preoccupation, feelings of guilt and ideas of persecution have also

been found to be suitable. Freeman (Freeman and Watts¹) has explained that the operation should be reserved for patients with severe and intractable mental symptoms, and that other methods should be tried first. Some, like Fleming, have not thought this precaution to be necessary. After-treatment has to be carried out with care, not simply from a surgical but from a psychological viewpoint. For a time after the operation the patient is sometimes a mere inert vegetable and may have to be trained again even in the simplest functions. It has been noted that excessive cheerfulness after the operation may be an indication that not enough fibres have been cut. Occasionally the patient is more tiresome after the operation than before it. 'Washing mania' is said to be relatively uninfluenced after the operation, although the anguish may have departed. Hallucinations and phobias tend to die out because, although they may persist for a time after the operation, they have lost their effective reinforcement. The chief histopathological change after the operation is a degeneration of the dorso-medial nucleus of the thalamus. Some patients are able to resume their previous occupations after an interval proportionate to the intricacy of their work (Freeman and Watts²).

A survey of operation results in the United States of America and in Canada has been made by Ziegler. Of 618 patients operated on, 12 died as a direct result of the operation and 18 subsequently; 214 recovered after the operation; 194 were clinically much improved; 109 were slightly improved; 62 were unimproved and 8 were worse. Of those who had recovered the majority were working full or part time. When one considers the apparent hopelessness of most of these cases the results are impressive.

Genetics

The theory of the mode of inheritance of the commoner psychiatric conditions is still in a very speculative state as is shown by the almost complete reversal of previous hypotheses that has taken place and the diametrically opposite views held by authorities in this field. The contortions of these experts tend to remind us of Mr. Churchill's description of a certain political opponent as a 'boneless wonder'. Kallmann continues to maintain that schizophrenia is dependent upon a recessive unit character. Slater³, on the other hand, reminds us that the most progressive geneticists have given up the idea of unit characters. He quotes Huxley to the effect that 'to-day the notion of Mendelian characters has been entirely dropped'. On the theory of recessive inheritance Slater remarks that 'it is impossible to explain Kallmann's findings without a quite unlikely intensity of in-breeding among schizophrenic gene carriers'. Slater prefers a hypothesis of 'simple dominance'.

War psychiatry

The chief trends in war psychiatry at the moment might be summarized as follows.

(1) The recognition of the importance, but at the same time of the difficulty, of selection procedures in cases in which temperament and liability to psychological breakdown are concerned. For reasons of security little can be published on this topic while the war lasts. Probably the best work that has been done in this field in the Allied countries is that on officer selection in the British Army (Rees). As regards one aspect of the difficulties in selection, Hitschman and Yarrell noted that the majority who became ill with psychoses two months after induction were apparently well adjusted before enlistment, and in their opinion even the most careful psychiatric examination would not have detected these cases. Hitschman and Yarrell recommend therefore a three-month preliminary training period before complete enlistment, partly to save the Government from incurring a responsibility for pensions afterwards. It is claimed that the majority of psychoses occur in the first two months of service. In order to eliminate the majority of severe neurotics, however, a considerably longer probationary period than this would have to be adopted.

As regards the criteria of psychiatric fitness for the Forces, volunteering, in the United States of America at least, appears statistically speaking not to be a favourable omen but rather the reverse. Thus it has been noted that people with psychiatric abnormalities such as alcoholism, epilepsy, schizophrenia and psychosomatic disorders of the gastro-intestinal type, are relatively more numerous among volunteers in the United States of America than they are among conscripted men, whereas psychoneurotics other than those with gastro-intestinal symptoms, psychopathic personalities and feeble-minded individuals tend to avoid service. The use of psychiatric questionnaires has been developed during the present war and Flicker gives a sample questionnaire

of this kind. It does not appear, however, that a questionnaire can satisfactorily reduce the proportion of enlisted men who require to be seen by the psychiatrist to less than about 40 per cent.

(2) Considerable emphasis has come to be placed on physical methods of treatment in war neuroses. Thus Sargent quotes Craigie who 'compared the urgency of treating with adequate deep sedation an acute neurosis in a good personality starting to break down to the urgency of operative intervention for correction of an acute condition within the abdomen'. This rather dramatic statement is not borne out by everyone's experience unless the term, sedation, is widened so as to include removal from the battle area to some suitable environment with well-trained staff to see that the patients get enough rest and nourishment and that their lives are well organized, coupled with a certain amount of simple psychotherapy. The difference probably hangs partly on the definition of the word 'acute'. Patients who show recent acute anxiety syndromes should be given sedation, if necessary up to the degree of continuous narcosis, for several days; this at least should tend to shorten the duration of the subsequent illness. How far it prevents the development of a chronic condition is dubious, for what seems to be the really determining factor in the ultimate prognosis is not the severity of the experience but the previous personality. Indeed a claim does not appear to be made even by the most enthusiastic advocates of intensive sedative treatment that it enables individuals of originally inadequate personality to return to front-line duties (Sargent).

The insulin sub-coma method has been found useful in diminishing anxiety symptoms, especially in patients whose anxiety expresses itself in physical discomforts and complaints; it is claimed that it is useful whatever the psychiatric basis for the anxiety symptoms, that is to say whether they occur in a psychoneurotic or a psychotic setting. Recently a combination of sedative methods, by the administration of sodium amytal for the greater part of the time and sub-coma doses of insulin in the mornings, has been thought to be helpful (Sands).

Sometimes the employment of these methods, however, merely makes the patient more anxious. Their tangible and even dramatic nature constitutes a temptation to use them as a routine, especially when large numbers of patients have to be treated. There is a danger that the simple but usually more fundamental psychotherapeutic method may be neglected, with detriment to the ultimate results in terms of Service usefulness.

(3) The differentiation of clinical syndromes which result from battle experiences has engaged the attention of a number of observers. In particular the 'traumatic' type of neurosis, in the sense of psychoneurosis ensuing on psychological trauma, has engaged attention. Most observers record as typical of this reaction recurring anxiety dreams and heightened irritability, especially in the form of a 'startle' response. 'Startle' response is probably only one manifestation of a generalized heightened irritability (Rome). Smith adds to the above list the conditions of over-susceptibility to alcohol and of emotionalism. This syndrome in fact has distinct resemblance to the 'hyperaesthetic-emotional state of weakness' described long ago by German authors or what would have been called in English psychiatric literature a 'neurasthenic' state supervening after some severe physical illness. The resemblance of the psychoneuroses which result from psychological trauma to the effects of fatigue are striking. The difference is possibly mainly in the aetiology of the so-called traumatic psychoneurosis which is produced suddenly and not as a result of fatigue, but even this distinction may break down in that it seems very difficult to distinguish systematically between some war neuroses of gradual onset and others with the classical sequence of sudden fright and subsequent neurotic symptoms.

Symonds has again drawn attention to the latent interval which is often observed between a frightening experience and the onset of actual symptoms and has sought to explain it on a neurological analogy; he points out that there is no conscious fear at the time, presumably because although there is a central excitation the central inhibitory processes for the time being prevent the translation of this excitation either into conscious or into peripheral manifestations. There are however instances indistinguishable from the rest in which conscious fear appears to have existed from the start. Inhibition appears to depend partly upon the exercise of voluntary effort during the traumatic period. For example, it has been remarked of shipwrecked survivors in life-boats that they appear to keep themselves well in control until safety is reached but that then anxiety attacks with trembling, sweating and so forth, develop (Bellamy).

Hoch gives a useful classification of the different sorts of emotional reaction to danger as (1) an 'emotional storm' showing itself in manifestations of terror; (2) a 'motility storm' in the shape of trembling and other uncontrolled movements; (3) a 'vegetative storm' in the form of visceral symptoms of anxiety. Stephenson and Cameron approach the problem of war neuroses from the point of view of development in time. They distinguish a phase of early stress in which the mood is one of anxious expectancy which leads to a second stage of 'established tension' with bodily signs of apprehension and finally to the third phase which they call 'anxiety' in which depression, exhaustion and loss of weight are very prominent. This sequence, as far as the third stage is concerned, is not often seen, but depression can sometimes become the predominant feature in a man who has struggled for a long time against his anxiety. Depression is often determined partly by a sense of failure. Depressions however are more often seen as immediate constitutional responses to stress than as sequels to a long established anxiety syndrome.

As there is a risk that physical methods of therapy may be overdone to the neglect of psychotherapeutic methods, it is worth noting that sedatives have been found to be disappointing in panic (Brosin) which is better tackled by simple psychotherapy. Parfitt and Gall have called attention to the fact that amnesia patients can usually—and indeed in the authors' experience can always—be cured by psychological means without the use of the popular method of intravenous injection of a barbiturate which is such a tempting short cut. The choice of method should probably depend upon the acuteness of the symptoms and upon the facilities available; when there is time, the purely psychological method is preferable; when there is acute distress, the narcotic method may be useful in the mitigation of the mental pain of recovering the repressed experience.

The neglect of hypnosis in the treatment of war neuroses is discussed by Fisher. He quotes Hadfield who points out that there are many who object to 'the needle' and that the use of intravenous barbiturate is a relatively crude method of treatment.

Incidence of war neuroses

Whitby, from an experience of general practice during the time of heavy raids on London, concluded that there was a small but real increase in nervous symptoms in the available population; over the whole period the incidence of such symptoms was gratifyingly low.

Surgical operations among psychiatric patients

Contrary to general belief it has been found that the frequency with which patients with psychiatric disorders who have functional bodily symptoms are exposed to surgical operation is but little greater than is the incidence of surgical operations in a control group. The bodily regions in psychiatric patients which have been most suspect of having surgical disorders were the rectum, the pelvis and the thyroid gland. In a survey of seventy thyroidectomized patients in whom psychiatric disorders developed, Howard and Ziegler noted that the relation of toxic goitre to psychiatric disorders was questionable except in the deliriums due to acute hyperthyroidism. They record the history of one patient who became psychotic just before he was to have a thyroidectomy; he received electrical convulsion treatment, after which the metabolic rate promptly fell. It should be noted, however, that the metabolic rate was already falling before the electrical treatment was given. It has been observed in Great Britain (Batt²) that in hyperthyroid patients with psychotic manifestations the hyperthyroidism may subside completely after electrical convulsion therapy.

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NEUROLOGY

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THE YEAR IN RETROSPECT

A pronounced tendency during the past year has been to give increased attention to what is called psychosomatic medicine. This term is held to embrace all diseases in which there are both mental and physical elements, and so it has been applied to several groups of conditions. There are first of all denoted as psychosomatic *symptoms* certain abnormalities which are due to organic brain disease in which the mental concept of the scheme of the body is disturbed, and in regard to these the word, psychosomatic, is used perhaps in its purest sense. The next group is composed of those conditions in which, in association with symptoms that are predominantly mental, certain physical disturbances occur; the best example of such conditions is the occurrence of bodily disturbances in association with psychotic depression. The conditions in the third group are chiefly manifestations of physical disease in which emotional factors have been postulated; asthma and angina pectoris may be cited as examples of this group; it is this group of diseases which has recently aroused a new attention. The conviction has been strong among medical officers of the Forces that certain physical diseases—duodenal ulceration for instance—were probably in some degree due to the anxiety which was almost constantly an associated condition, and thus impetus has been given to a movement which was slowly gathering strength before the present war. The tendency is to enlarge this group greatly and to attribute to emotional factors a share in the causation of a very large number of physical complaints; there is in consequence among physicians a greater recognition of the part which the nervous system plays in controlling the structures of the body and in maintaining their health. There remains a fourth group of conditions in which the symptoms are partly physical and partly mental as a result of organic brain disease, for example general paralysis of the insane and Huntingdon's chorea.

Psychosomatic symptoms of the first group were referred to in some detail in Medical Progress (Critical Survey section) 1943, p. 73, and increased attention continues to be paid to them. In the second and third groups the autonomic nervous system is intimately concerned. The range and degree of physical changes which may be brought about through the medium of the vegetative nervous system as a consequence of the action upon it of frequently recurring emotion are still very imperfectly known. The present tendency is probably to exaggerate the degree of physical change that is capable of being produced in such a way. It may also be that some of these conditions are not actually psychosomatic, but are rather neurosomatic in the sense that the activation of the autonomic centres in the central nervous system may not always be emotional but may be of a more organic nature. In this connexion it will be recalled that some years ago Beattie and his co-workers found that gastric and duodenal ulcers occurred very often in experimental animals when lesions had been made in the hypothalamus.

Research in psychosomatic problems

Such a trend is bound to bring into greater prominence the influence of the autonomic nervous system as the connecting link between *psyche* and *soma* and to cause greater concentration on the study of its functions. In the United States of America, where the range of vision is wider than it is in this small island, a Society for Research in Psychosomatic Problems has already been formed with America's foremost neuropsychiatrist, Dr. Adolf Meyer, as Honorary President, and another of her foremost neurologists, Dr. Tracy Putnam, as executive President. The Society has appointed ten committees, destined to study the individual from the moment of conception until the end of his working days. The first committee is concerned with psychosomatic problems in obstetrics and gynaecology, the second with those in infancy and childhood and the

tenth with those in industrial medicine. Another committee is concerned with psychosomatic problems in war medicine and still another with the psychosomatic approach to social and cultural problems. Among the diseases which psychosomatic medicine takes within its province may be mentioned angina pectoris, coronary thrombosis, arterial hypertension, asthma, migraine, nervous dyspepsia, gastric and duodenal ulcer, vaginismus and eczema. Probably the greatest mistake is to attribute too much to the psychological factor—clear thinking is nowhere more strictly called for than in this department of Medicine.

Neuropsychiatry

An important problem that has now arisen for neurology is that of its relation to sister sciences—whether it is going to adhere to general medicine on the one hand or to psychiatry on the other. Several factors have combined to bring this question to a head. The most urgent is perhaps the apparent imminence of a State medical service which will require the appointment of a number of neurologists and will demand certain qualifications from the candidates for such appointments. The matter has already been focused by the attitudes of the different fighting forces towards medical neurology. In the Royal Air Force—in which it was recognized in pre-war days that there were many psychological problems, and where there was at the same time an obvious need for a neurologist to deal with cases of spinal and cerebral injuries and with peripheral nerve injuries—it was decided to establish a service of neuropsychiatrists. This seems to have worked very happily and to have been the most successful of such organizations in the British fighting forces. In the Royal Navy a smaller number of neurologists and neurological surgeons and psychiatrists were appointed, and an attempt was made to divide the province between them; the success of this arrangement must be regarded as doubtful. In the Army, at the outbreak of the present war, the sphere of psychiatry was for the first time regarded as important. It was thought that psychiatrists would cope with all the functional nervous cases and a neurosurgical organization was set up which was to deal with all the cerebral and spinal injuries; no medical neurologists were appointed. In spite of the fact that extensive use was made of the Emergency Medical Service and its staff, it was found necessary after a year or more to appoint a small number of medical neurologists; this number has been gradually increased and is now represented in all the important military areas. An attempt was made to limit the province of the neurologists strictly to cases of recognized organic nervous disease, which resulted inevitably in great impairment of their usefulness and a considerable degree of confusion among unit medical officers who followed their peace-time practice of referring all cases of nervous disease to the neurological specialist. A third cause of the present dilemma lies in the development of neurology itself and to a less extent in recent trends in psychiatry. With the advance in knowledge of cerebral function, mental symptoms are becoming more and more recognized and more and more important, and the organic neurologist must, for this reason alone, have more training in psychology and psychiatry. On the psychiatric side, the complete failure of psychiatric methods to deal with the major psychoses has led to the adoption, with no small degree of success, of some rather desperate physical measures, of which convulsive therapy is the most used and the operation of prefrontal leucotomy the most drastic (see *Surveys and Abstracts* 1941–2, p. 81).

In spite of the unfortunate position which has been taken in the British Army and of the uncompromising attitude of certain psychiatrists—who consider that psychiatrists alone should deal with all nervous conditions of a functional nature—it seems inevitable that neurology and psychiatry should be drawn more closely together and, as has been said in the foregoing paragraph, it is apparent that both must become more closely integrated with general medicine. It also seems inevitable that after the war there will be a strong revival of the study of abnormal psychology based on organic brain disease.

ANATOMY AND PHYSIOLOGY

Regeneration within the central nervous system

It is generally held that, whereas regeneration of nerve fibres takes place in the peripheral nerves, regeneration does not occur in the spinal cord or brain. I have elsewhere given reasons for supposing that regeneration does occur within the spinal cord. The

optic nerve is not of the nature of a peripheral nerve but is rather a tract of the brain which reaches out to make contact with the mesodermal structures which form the eye. Sperry has shown that in amphibians the divided and partly removed optic nerve regenerates and makes a new connexion with the brain and that vision is regained in consequence. In the frog the degree of vision restored may be such that little difference between the behaviour of the animal operated on and that of control frogs may be observed. The frog which has been operated on is capable of seeing and pouncing upon a fly at a distance of 35 centimetres, which is normal for the species concerned. If at the time when the optic nerves are divided each eye is rotated through an angle of 180° , the reactions of the animal after restoration of its vision indicate that it has a false projection: it interprets objects seen actually with the lower half of the retina as being low down, that is as if they were seen with the upper half. This shows (1) that the function of localization remains in the retina and (2) that the regenerating fibres regain approximately their original anatomical relation but not their original functional connexion. This work seems to open up a new field in the investigation of the powers of regeneration of cerebral tracts in different species and under different conditions and seems certain to lead to much more work.

INCREASING KNOWLEDGE OF THE CEREBELLUM

Although there is a good deal of knowledge of the functions of the cerebellum, knowledge of its precise anatomical connexions is still very imperfect. During the current year Adrian and also Dow and Anderson have brought forward further evidence of functional localization within it and of various stimuli reaching it from the limbs. These must obviously travel by way of the direct and indirect spinocerebellar tracts.

Afferent stimuli

When the cerebellum is exposed and needle electrodes are led off from the area of the culmen continuous variations of potential can be recorded. The intrinsic activity of the cerebellar cortex is shown by small potential waves of high frequency (150–250 per second) and these are increased in size and frequency by afferent discharges. The arrival of such discharges can be recorded by means of a wire electrode at a depth of about 1.5 millimetres from the surface; by such a method it is possible to make a map of the regions connected with different parts of the limbs and body. In the cat and the monkey, spinocerebellar discharges from the hind limb arrive in the lobulus centralis on the same side. Discharges from the fore limb arrive behind them in the culmen, and in some animals discharges from the vibrissae of the snout are found still further back in the lobulus simplex. The afferent areas for the different limb segments are in the order of hind-foot, leg, hip, shoulder, forearm, fore-foot. The commonest peripheral discharges which reach the cerebellum come from pressure receptors in the feet and receptors in joints and muscles. Dorsiflexion at the wrist or ankle, combined with pressure on the sole of the foot, is a most effective stimulus. A single afferent unit in the cerebellum may be connected with receptors as far apart as the toe and the heel.

Other afferent stimuli, those which reach the cerebellum by way of the pontocerebellar system, have also been studied. They are derived from the cerebral motor cortex; those from the cortical areas corresponding to the hind limb, fore limb and face reach the lobulus centralis, culmen and lobulus simplex respectively, on the opposite side.

The receiving areas overlap those for the spinocerebellar discharges and extend farther out laterally.

It thus seems clear that afferent discharges from a limb will cause increased activity in a localized area of the cerebellar cortex, and that discharges to the limb from the motor area of the cerebral cortex will cause increased activity over a wider area in the same part of the cerebellum. The increased activity is likely to produce a temporary lessening of extensor tone.

Efferent stimuli

A puzzling feature is that the arrangement of the afferent 'limb areas' in the cerebellum as shown by this series of experiments is exactly the reverse of that indicated by other experiments made by Connor and by Connor and German when they studied the efferent connexions by the method of localized ablation.

Most of Adrian's experiments were made when he was ignorant of Connor's work,

but the localization found in the latter has been checked repeatedly. The present position thus is that whereas sensory messages from the hind limb arrive in the cerebellum in a region anterior to that for messages from the fore limb, the region controlling the hind limb is posterior to that controlling the fore limb. Can it be that a motor discharge for the fore leg causes diminished extensor tone in the hind leg and vice versa? It seems to be improbable, but obviously much more evidence is required to prove or to disprove it.

HEAD INJURIES

Ventricular dilatation

It has been known for several years that dilatation of the ventricles of the brain may occur after cerebral injury, and in general this has been interpreted as indicating an atrophic process affecting the cerebral hemispheres. A paper by Davies and Falconer analyses a series of 100 cases observed at the military head injuries unit at Oxford, and correlates ventricular dilatation to clinical findings.

The dilatation may affect both lateral ventricles, one lateral ventricle or only a part of one ventricle. The proportion of cases in which ventricular dilatation is found increases with the severity of the trauma. The dilatation does not appear to be influenced as much by the site or direction of the violence as by the presence of a fracture of the skull; focal dilatations in particular tend to develop beneath the site of localized fractures. These ventricular enlargements first appear within two or three weeks of injury; such evidence as is available indicates that the maximum is reached in about four weeks and that the condition then persists unchanged.

There were seven cases at Oxford which were examined within a month of injury and were re-examined at later dates. In no case was there evidence of progression of the ventricular enlargement later than from four to six weeks after injury.

In most cases there is an obvious relation between the ventricular dilatation and the clinical signs. Patients with residual pyramidal signs on one side of the body are usually found to have dilatation of the lateral ventricle on the opposite side of the brain. In other cases, patients who do not present any residual clinical signs but who are known to have shown signs of pyramidal disturbance in the acute phase of the injury, often show similar enlargement of the contralateral ventricle. In patients with noteworthy intellectual and mental deterioration both ventricles are often enlarged, whereas in those without objective deterioration and with disorders merely of a subjective character such as headaches and dizziness, the ventricular system is more often normal. Post-traumatic epilepsy does not seem to be connected with changes in the ventricular outline.

The authors conclude that focal dilatation of a ventricle results from atrophic processes associated with the resolution of local pathological changes such as haemorrhage, contusion or laceration. They do not come to any decision regarding the mechanism of the more usual generalized dilatation, unilateral or bilateral, yet there seems to be little doubt that this also has its origin in atrophic processes which are of wider distribution.

POLIOMYELITIS

Bacteriology

Rosenow has put forward in various writings the theory that the filtrable virus which is responsible for the propagation of poliomyelitis under experimental conditions represents a phase in the life cycle of a streptococcus.

He believes that the streptococcus which he has isolated from the nasopharynx and tonsils of patients during life, and from emulsions of the brain and spinal cord after death, plays the primary part in the causation of the disease, in the occurrence of epidemics and in the production of immunity, during the period in which the virus is in its small filtrable, highly invasive and relatively non-antigenic phase. For this very important hypothesis Rosenow brings forward a mass of evidence of a bacteriological and experimental nature.

Monkeys which recovered from paralysis after inoculation with the streptococcus became immune to poliomyelitis virus.

By the use of autoclaved dextrose-brain broth and soft dextrose-brain-agar in tall tubes, this same type of streptococcus has since been isolated consistently from the nasopharynx, tonsils, stools, cerebrospinal fluid, brain and spinal cord. This has been

done during studies of altogether thirty-seven widely separated rural or urban epidemics and seven institutional outbreaks of poliomyelitis; the material studied came from the cerebrospinal fluid or the brain and spinal cord of more than 400 monkeys which had succumbed to poliomyelitis after inoculation with many different strains of virus.

The streptococcus, although of low general virulence, was found to have specific affinity for the anterior horns of the spinal cord on appropriate inoculation, producing, as the outstanding manifestation, flaccid paralysis in guinea-pigs, rabbits and monkeys. Monkeys which recovered from paralysis after inoculation with the streptococcus, and those which were thoroughly vaccinated with the poliomyelitis streptococcic vaccine, often became immune to virus.

This type of streptococcus has been shown to be present constantly in the nasopharynx of human beings while they were ill with acute poliomyelitis.

Precipitation tests made with the poliomyelitis antistreptococcic serum and the serum of human beings and monkeys, and cutaneous tests made by intradermal injection of the euglobulin fraction of the antistreptococcic serum, have shown that a poliomyelitic-streptococcal antigen appeared in the serum and skin of nearly every one of 324 persons and 170 monkeys while they were ill with epidemic and experimental poliomyelitis. It was also found that the antigen persisted throughout the course of the disease. It disappeared gradually when recovery ensued, and promptly after the therapeutic injection of the poliomyelitis and antistreptococcic serum.

The protection of monkeys by immunization with different strains of the streptococcus and with corresponding vaccines, and the curative and neutralizing action of different batches of poliomyelitis antistreptococcic serum, have been demonstrated in a large number of experiments.

It has now been found that the many unsuccessful attempts which had been made earlier to produce typical poliomyelitis and transmissible virus in monkeys by the use of streptococci isolated in studies of poliomyelitis were due to the use of media which became acid from the growth of the streptococcus. In consequence of the use of a new medium extremely small filtrable forms and transmissible viruses developed from streptococci. This has occurred thus far in the case of each of six strains of 'neurotrophic' streptococci; three of these were from poliomyelitis and three from sources wholly unrelated to poliomyelitis or to encephalitis. The changes in size of the streptococci from small to large (virus to streptococcus) and from large to small and filtrable (streptococcus to virus) in the chick-embryo medium, without apparent change of antigenicity, resemble the phenomenon of polymerization in which great alterations of physical properties occur in certain substances without change of chemical constitution.

Monkeys which recovered from a paralytic poliomyelitis that developed after inoculation with 'natural' virus were immune to the various strains of adapted experimental and 'natural' virus and their serums neutralized these strains. Monkeys which recovered from paralytic poliomyelitis resulting from inoculation with experimental virus were immune to, and their serum neutralized, the experimental and 'natural' viruses.

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SKIN DISEASES IN WAR-TIME

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It is not always appreciated that disease and disorder in the skin are the outward and visible signs of disease or disorder affecting the patient as a whole. It is true that a few infections and inflammations which are caused by external influences are peculiar to the skin, although even these have their counterparts in the respiratory and gastrointestinal systems. Nevertheless, the majority of the ills presented to the dermatologist reflect the general health of the patient: they are evidence of disease of the organism as a whole or of disturbance of normal function in that organism. It would, indeed, be absurd to imagine that so vital an organ as the skin was divorced from the remainder of the organism, suffered its own peculiar afflictions and did not participate in the general health or ill health of the remainder. It is to be feared that in his student training and too often in subsequent practice the doctor regards skin disease as something peculiar, as something bearing little relation to general Medicine as he understands it. Much is lost to general Medicine and to dermatology by this odd point of view, and it is to be hoped that a revised medical curriculum will recognize the value of the skin which, alone among all the organs of the body, displays disease processes and functional disorders for direct observation, study and investigation. No doubt one of the major stumbling-blocks has been the fact that disorders of function in the skin are considered in terms of their objective manifestations, each pattern of reaction bearing a distinctive label, whereas the same disorders when they affect internal organs are visualized in terms of their subjective symptoms. The matter is worth careful study since much that is learned in relation to skin diseases can be applied with advantage to the internal organs. A knowledge of skin diseases helps the physician to retain a sense of proportion in regard to therapy, and is a useful check to the devastating enthusiasms which are apt to swamp the field of therapy from time to time as a consequence of fashion and fad and to obscure the general underlying principles which must be retained if practice is to be sound.

In the same way that the skin mirrors the health and the tone of the individual, it reflects the influence on him of social and economic changes, of psychological, nutritional, climatic and other factors. It is to these influences that attention at this time may be turned with advantage. A state of war brings with it profound changes in the social structure; the influence of community life is strong, psychological stresses and strains are in evidence, and the tempo and balance of industrial and of agricultural life are affected. These conditions must influence health and disease and they are naturally reflected in war-time diseases of the skin. Certain groups of such diseases are considered in the following pages.

PARASITIC AND SEPTIC INFECTIONS

Scabies

The incidence of scabies was increasing before the present war began but there can be no doubt that the effects of 'shelter life' in the larger bombed cities, the crowding together of evacuated folk and the conditions of life in the Forces have favoured the development of an epidemic such as we have rarely experienced. This has greatly stimulated fruitful scientific work; much is now known of the life cycle of the *Acarus* and a single and entirely effective treatment has been evolved (Mellanby). The essentials of this treatment are that a 25 per cent emulsion of benzyl benzoate is applied to the whole body except the head and face and is allowed to dry into the skin, and that bathing is suspended for forty-eight hours so that the emulsion is not washed out of the skin. All family and intimate contacts must be similarly treated at the same time.

It is established that signs and symptoms of scabies do not develop for six or eight

weeks after infection, and that intimate personal contact, not clothes and bedding, is the usual channel of infection. It has also been recognized that effective treatment of this community disease should be undertaken by the health authorities through the institution of clinics. A similar course and somewhat similar treatment is necessary for pediculosis capitis, an affection which has increased greatly among women largely because of fashions in hairdressing. Effective control of this pest calls for legislation extending beyond the individual and her home to the factory and hairdressing establishments.

Ringworm

Small-spore ringworm of the scalp in children under the age of puberty, which for many years has been almost non-existent in most areas, shows signs of considerable increase. Early detection by the use of ultra-violet light filtered through Wood's glass, if the method is properly employed, should control spread of this parasitic infection. All children in the family of and in the class or school attended by an infected child should be examined by this method. Treatment of children under five years of age by thallium acetate has proved to be of value in the hands of those who are familiar with the procedure; it should not be employed except by the expert. The same applies to epilation by means of X-rays which, by the introduction of a new technique, has brought the treatment to a level at which it is less liable—through minor errors or movement by the patient—to cause radiotherapeutic damage to the skin, with consequent baldness (Shanks).

Increased activity in agriculture and the evacuation of a considerable number of the population to the country have given rise to many more cases of cattle ringworm infection of skin and hair. Treatment is not very satisfactory and progress is slow. It can sometimes be hastened by the occasional application of derobin (dithranol) in the form of a paste, the ingredients of which are as follows: derobin 2 grains, salicylic acid 10 grains, zinc oxide 120 grains, starch 120 grains, soft paraffin to 1 ounce. This is the most rapidly effective measure in the treatment of ringworm of the groin (dhobie itch) which has been common in the Forces. It is applied for three days, during which baths are not taken, and then baths and soothing applications are employed in order to allay the reaction. Much work remains to be done in the field of parasitology—work which must keep step with a study of changes in the character of the soil in which fungus thrives. Immunity of the scalp to small-spore ringworm after the age of puberty suggests an endocrine influence, whereas the resistance to treatment of infections between the toes may be dependent upon the biochemical factors concerned. The incidence of the latter condition has greatly increased and it has appeared in the mining industry in which the opportunities for spread and the disabilities caused are considerable. The incidence of ringworm of the toes not only varies in different countries but also varies considerably in different parts of Great Britain. In general it is still restricted to a clearly defined stratum of society. It is recognized that a number of different fungi of the large-spore type may be responsible, and that in the chronic form there are other factors than mere infection which make it difficult to cure the disease. A chronic eczematization may be associated with the disease and phenomena due to secondary sensitization may appear, such as pompholyx of the hands. Many cases diagnosed as ringworm of the toes are, however, no more than hyperidrosis with simple pompholyx or with a condition in which the skin between the toes becomes sodden.

Septic conditions

Mention must be made of the increase of septic conditions of the skin which in part are no doubt secondary to the increase in parasitic disease. Treatment has been along the lines of sulphonamide therapy, used both internally and externally; more recently—on the experimental level—penicillin has been employed. Results are sometimes dramatic but it is more than doubtful whether sulphonamides should be used as a routine in the treatment of these common and simple ills, for the known dangers of the compounds are not inconsiderable and there may be dangers yet unknown. The development of sensitization to sulphonamides is more readily provoked by local application of the compounds to the skin than by oral administration and has more serious and disabling effects; it may also be complicated by light sensitization (Barber).

In general, simple non-irritant antiseptic measures, the keeping of affected parts dry and the use of dry heat are sound principles in the treatment of skin sepsis.

INDUSTRIAL AND CONTACT DERMATITIS

The field of industry has produced a variety of ills the study of which is most important in regard to general and social health. Much functional disorder and many symptoms of general debility have been consequent upon fatigue from working long hours and under unhealthy conditions (night work and black-out), from stress and strain, domestic and family troubles, travel and housing difficulties and altered habits in regard to feeding. In the skin such conditions of living have been reflected in increased pruritus and eczema, in seborrhoeic manifestations and in exacerbation of chronic ills such as psoriasis.

More particularly there has been a great increase in dermatitis arising from specific irritants and of non-specific dermatitis caused by dust or liquids. The increase has been dependent upon many factors of which the influx of new labour unused to factory conditions, the greater demands made upon regular labour and the introduction of new materials and processes have been the most important. With the progress of time a large amount of selection takes place, even in war-time, so that persons who are unsuited to certain trades are weeded out. The unavoidable use of some irritants has made necessary the development of improved processes of protection and of cleansing.

Oil dermatitis

In engineering, oil acne and folliculitis and oil dermatitis have been in large part controlled. Oil acne and folliculitis affects more severely the adolescent and the seborrhoeic subjects; oil dermatitis is more dependent for its occurrence upon irritants incorporated in the oils such as alkalis (in oil-and-water mixtures used for cooling and in drilling and turning) and sulphur. The thorough and complete removal of the oil from the skin after work by the use of some emulsifying cleanser—for example, a sulphonated castor oil with a 2 per cent wetting agent—will prevent the occurrence of a large number of cases. More sensitive persons may have to apply some additional protection to the skin—a barrier cream—before work, or they may have to give up work in the industry concerned.

Other irritant substances

For the protection of workers against irritant chemical powders such as those which are used for example in the manufacture of explosives and the filling of detonators and shells, the clothing, including a turban for the hair, is of a special character. Protection is reinforced by the use of rubber or other gloves and masks when necessary, but in the filling processes such protection is not possible. The face and hands are then shielded by the use of barrier creams and powders; the worker passes through a 'beauty parlour' for the proper application of these 'cosmetics' before she starts work.

The manufacture of plastics and their increasing use in industry is responsible for a certain amount of irritation which is sometimes produced by the formaldehyde used. The synthetic glues and resins are widely employed in aircraft and other industries and so is the 'bakelite' type of plastics. Dermatitis caused by the wearing of plastic spectacle frames is seen from time to time.

The use of chlorine in organic combination in a number of industries related to war work provokes a severe and acute outbreak of chloracne on exposed parts of the skin. This slowly clears when the patient is removed from the work.

Contact with metals in industry, metal dust and fumes, or metal in combination with oil—nickel, chrome, aluminium, brass and various alloys—may produce industrial dermatitis in those who are susceptible or in whom sensitization develops. Similar trouble is seen to arise from the wearing of metal suspenders, of metal fasteners to garments and of metal wristlets, necklaces and other objects. Avoidance of contact with or proximity to such metals alone will ensure recovery from the troublesome effects.

The problem of the prevention of dermatitis which is caused by external irritants is one that presents very many different aspects and approaches and calls for serious scientific research. The protection of the worker by the application to the skin of bland impervious barriers has received much attention. These must not irritate the skin, must be insoluble in oil, water or other substances with which the worker comes in contact and must be easily applied and easily removable. The majority contain some inert powder and the preparation when applied leaves an invisible film on the surface of the skin (Ministry of Labour and National Service *Memorandum*).

Specific sensitization

There has been unquestionably an increase in the number of cases of dermatitis dependent upon the development of specific sensitization to particular contacts. The war conditions of manufacture have no doubt been responsible in part for the increase in dermatitis caused by the wearing of dyed fabrics, including articles such as socks and shoes, and especially of khaki. Dermatitis produced by the use of cosmetics and by contact with rubber, including rubber gas masks, also may be in part dependent upon war conditions of manufacture. The diagnosis of such conditions should not be difficult; the site of the eruption is related—often exactly—to the site of contact with the agent causing the eruption. Evidence of intolerance, although in some cases it may be delayed, may follow the first or an early contact with the garment or article concerned.

Treatment by desensitization is not effective and contact with the causative agent or with allied substances must be avoided. Sometimes a contact dermatitis increases sensitiveness to other irritants such as those caused by friction, light and exposure, and the disability may be prolonged.

Light-sensitiveness

Apart from association of the kind mentioned above, however, the incidence of light-sensitiveness itself has increased during recent years. The sensitiveness is to actinic light in most cases and affects exposed parts, particularly the 'flush area' of the face and the backs of the hands; it often causes oedema and much irritation and the development of a thickened, coarse eczematization of the parts, which present a scrubbed appearance. Whether the increase of light dermatitis is a natural phenomenon or whether it is related to altered diet or to other temporary conditions of living is difficult to ascertain. We know that certain drugs and toxins in the blood stream may cause light-sensitiveness and that lack of certain essential foodstuffs may also do so. Light dermatitis is mostly to be observed between the months of February and October.

Protection has been afforded in a few instances by the use of concentrated esters of the vitamin A fraction of certain fish oils given by injection, but it is generally necessary to provide some mechanical or physical protection—something that will absorb the light rays—to exposed areas of skin. Titanium dioxide (which is contained in the preparation, Siccolam) or a calamine foundation lotion applied under an ichthammol dusting powder are valuable protectives; tannic acid and quinine are sometimes effective since they are opaque to certain light rays.

PSYCHOGENIC DERMATOSES

Wars and rumours of wars are the cause of much emotional unrest, worry, anxiety and fatigue and of diverse stresses and strains. In no field of Medicine is this more readily reflected than in that of dermatology. In war-time, dermatoses are as a consequence one of the major sources of disability in the armed Forces and in civilians. Much of the industrial dermatitis that is seen is essentially dependent upon such factors, and no doubt they play some part even in the development of specific sensitization to particular irritants.

A review of the major dermatoses which cause disability in and discharge from the armed Forces gives a fair indication of the type of lesion commonly caused by psychological disturbance. These constitutional disorders although dependent upon a number of environmental influences—for example change of routine, diet and clothing—are chiefly to be related to the emotional disturbance occasioned by leaving home and civil contacts, and by the necessary adjustment to conditions of life in the Forces and to the purposes of service in them.

Itching of the skin and eczema of constitutional pattern are common symptoms. Some trivial injury or contact may determine the onset but the course of the affection is determined by failure or success in adaptation to the new life.

Seborrhoea

A most important group of dermatoses in the above connexion is, however, that of the seborrhoeic affections. Too much emphasis is laid upon the factor of infection by organisms in considering seborrhoeic ills. In fact, the latter are always dependent in the main upon constitutional disturbances—endocrine, metabolic, psychological. As

a consequence acne vulgaris, seborrhoeic eczema and sycosis barbae are major causes of disability in war conditions. It is admitted that many factors play a part in and many influences affect the aetiology of chronic seborrhoeic ills and that, evidences of imbalance having been established in the form of eczema or sycosis, it is difficult to restore the equilibrium which determines complete recovery. Weeping eczema of the head and ears and of flexures and eczema associated with sycosis are the most troublesome affections. Alkalinization and vitamin B therapy are important measures in treatment, and the aniline dyes, especially in an emulsified ointment base, are a help when applied locally. In some phases the use of sulphonamides by the mouth—not as external applications—assists control of the disease but physical and psychological adjustment to environmental conditions remain the determining factors in cure. Seborrhoeic subjects are unsuited for the life in tropical climates, for work in mines or with furnaces and for work in industries which are associated with vigorous exercise, heat, sweating and friction. These subjects are individualists and have to be managed as such.

In this group too are the cases of disability resulting from hyperidrosis of hands and feet, sometimes associated with livid erythema and sensitiveness of the skin; such patients are commonly subject to eczema of the pompholyx type. The emotional factor is always predominant in these cases and small doses of sedatives or sedative-tonics given together with vitamin B are important measures in treatment after the correction, as far as is possible, of emotional difficulties. Locally small doses of X-rays may control much of the trouble but they must be employed with care.

Psoriasis

Very similar considerations to those noted above in relation to the seborrhoeic patient apply to the psoriatic subject. Extreme heat and sweating are harmful, but the problems of psychological adaptation and adjustment provoke most of the distressing exacerbations to which this subject is susceptible. The eruption itself is a source of great distress because of its emphatic characteristics and the social embarrassment it carries with it. A vicious circle is readily established, and again the person who is very prone to psoriasis has to be regarded as an individual who cannot subscribe easily to community life. The affection can readily be cleared by treatment with sunlight after tar baths in hospital and the application of two grains of dithranol to the ounce of Lassar's paste. In subsequent management of the case, the problem of first importance is the control of relapse. Climatic and geographical considerations are important, as are the character of the patient's work and his emotional and nervous relations in his home and in other private and public activities as well as in his occupation.

Alopecia

Alopecia areata, another pattern of reaction to environmental maladjustment, is less common than is the eczematous, seborrhoeic or psoriatic pattern. Nevertheless it is seen both in the Forces and in civil life and, as with the other ills mentioned, there may be a familial predisposition to react according to this pattern. Although a source of embarrassment, it is a less serious disability than are the other lesions (Hellier).

ENDOCRINE FACTORS IN DERMATOLOGY

The element of endocrine imbalance is recognized to play a part in the aetiology of many dermatoses, particularly in acne vulgaris and in rosacea. In large part acne vulgaris, according to Barber and Bishop, is to be regarded as a male characteristic, is dependent upon an excess of androgenic hormone in the circulation and is to be corrected by the administration of oestrogen. Flooding of the circulation with oestrogen will produce dramatic improvement especially in severe acne in precocious youths; it is a measure likely to form part of the routine treatment of acne when further work has established the safe and desirable range of such therapy (Ingram). • •

EXPOSURE

Immersion foot

Trench foot was a major problem in the war of 1914–18, and the allied conditions of 'immersion foot' which is seen in shipwrecked sailors and airmen and of the 'shelter foot' which is seen in civil practice have led to fresh interest in and investigation of the problem during the present war (Greene). In this condition and in frost-

bite it is established that rest, absence of injury and of friction and avoidance of strong applications—especially of heat—are of first importance in treatment. Much damage and loss of limb and of life may be caused by neglect of these principles.

CONCLUSION

In this survey an attempt has been made to indicate how intimately dermatology reflects the health and mental tone of the patient and the social and economic influences which bear on the community. Great attention is being given to social medicine and to the importance of environmental influence upon health and happiness in the modern approach to Medicine. As has been shown above in relation to life in industry and in the armed Forces, the skin is a sensitive barometer in this regard.

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TROPICAL MEDICINE

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MALARIA

Incidence and prevention

Malaria is still the most important tropical disease from the point of view of the present war. Collignon has reported that the epidemic of the previous year did not recur in Algiers in 1940 because the conditions were unfavourable and the anophelene prevalence was much lower than the normal. In Greece Pampana records that the Rockefeller Foundation showed that summer epidemics of the malignant tertian form occur after heavy rainfall; they are aggravated by movements of population due to war or to other causes. In Yugoslavia Pampana reports that malaria is prevalent except in some high altitudes; it is most prevalent in the Danubian plain and the serious malignant tertian form is carried by *Anopheles superpictus* and is favoured by winter snows and copious spring rain. The most effective preventive measures are the control of the breeding of anopheles in the valleys, the introduction of the small *Gambusia* minnows into waters and the rendering harmless of anopheles-breeding watertanks by means of screening. In China Yao records that in 1939 thousands of workmen employed on the Yunnan-Burma railway died of malignant tertian malaria. In this region *Anopheles minimus* is the chief carrier, as it is in Assam.

Simmons reports that in spite of the enormous increase in the size of the United States Army, the malaria rates have been kept down by anti-mosquito campaigns in Army camps in the United States of America, in Panama and in the Philippines. The spraying of houses for the purpose of destroying infected anopheles is being increasingly relied on as an anti-malarial measure. For this purpose a new type of self-propelling insect spray, the Freon bomb, is being used against both mosquitoes and flies in United States Army camps. The bomb contains pyrethrum 20 per cent dissolved in Freon 12 at a pressure of 85 pounds to the square inch. When the nozzle is opened a fine spray emerges from the bomb which should suffice to kill all flies and mosquitoes in a space of 100,000 cubic feet (Article, *Soap*¹). In South Africa Russell and his colleagues report that in rural agricultural areas the only cheap and popular anti-malarial measure is to spray the village houses, which costs a quarter of a rupee (4d.) per head per annum. In some places the cost of antilarval maintenance measures has been reduced to less than 2d. a head but the initial outlay is heavier. Pyrethrum for use in the sprays should be grown locally.

When anopheline control is impossible drug control is advocated by Clark who advises the use of 0.1 gramme of atebirin (mepacrine hydrochloride) three times a day or of 18 grains of quinine daily in tablets, for five days. The Surgeon General of the United States Army has also issued very similar instructions for the drug control of malaria for the use of troops operating in malarious countries. It should be continued with adequate medical care until the men arrive at a base because the drugs have a suppressive action only while they are being taken—a matter of the greatest practical importance during active operations under conditions not permitting of control of anopheles carriers.

Plasma transfusion malaria

The danger of transmitting malaria through the transfusing of the blood of a malarious subject is well known. Lozner and Newhouser have tested the effect of using blood plasma for malarial therapy. The only two patients certainly infected with malaria were infected as a result of the use of plasma preserved in the liquid state for only one day; liquid plasma was harmless when it had been preserved for two weeks. Dried plasma was also safe.

Treatment

Totaquine, as recommended by the Malaria Commission, League of Nations, should

contain not less than 15 per cent of quinine. In view of the shortage of quinine during the war Seeler and his colleagues have studied in duck malaria the relative value of the different cinchona alkaloids. They found quinine, quinidine, cinchonine and cinchonidine to be of about equal activity, but quinoidine was considerably less active against malaria than were the crystalline alkaloids. Consequently the United States Pharmacopoeia has re-defined totaquine as a mixture containing not less than 7 per cent or more than 12 per cent of anhydrous quinine, and a total of not less than 70 per cent or more than 80 per cent of anhydrous crystalline cinchona alkaloids. Hawking reports that mepacrine hydrochloride given intramuscularly is rapidly absorbed; it produces locally only one-third as much necrosis as quinine does.

KALA-AZAR

Diagnosis

The complement fixation test, using the Witebsky, Klingenstein and Kuhn (W.K.K.) antigen, has been reported by several workers to be diagnostic of both cutaneous and general leishmaniasis. Sen Gupta has obtained positive reactions in 172 out of 177 cases of kala-azar (97 per cent); negative results were obtained in 262 cases of other diseases, with the exception of one case of chronic tuberculosis. The test was positive in twenty-one of twenty-two kala-azar cases when the disease was at too early a stage for the aldehyde test to be made; as recovery takes place the reaction tends to become negative. Lepromatous leprosy also gives positive reactions but only the post-kala-azar dermal form of leishmaniasis can be mistaken for nodular leprosy.

Treatment

The diamidines—and especially stilbamidine (4:4'-diamidinostilbene)—continue to be reported on favourably in the treatment of kala-azar. Kirk and Sati report later results in forty-four cases of the resistant Sudan form of kala-azar with a case mortality of 18 per cent; five of the eight fatal cases had been admitted in a very advanced stage of the disease. Of thirty-six patients discharged provisionally as cured observation of thirty-two has been continued of whom three are known to have died and twenty-eight were in good health two and a half years later. Napier and Sen Gupta report on thirty-two cases which were treated with 4:4'-diamidinodiphenoxypentane (pentamidine) with nineteen of twenty-one ordinary cases cured and ten of eleven resistant cases cleared up; it is too early to say whether or not the patients are all permanently cured. The doses were very similar to those of stilbamidine given in Medical Progress (Critical Survey section) 1944, p. 98.

LEISHMANIASIS, CUTANEOUS

The local injection of solustibosan (pentavalent antimony hexonate) in cases with not more than three sores is recommended by Vilanova. Up to a total of 2 cubic centimetres of a solution of 100 milligrams per cubic centimetre is injected at one sitting; there is some pain, but the parasites all disappear within twenty-four hours and healing of the sores with little scarring ensues.

YELLOW FEVER

Epidemiology and distribution

Now that yellow fever is known to be widespread in the western portions of East Africa the possibility of a disastrous spread under war conditions to south-west Asia and to India has to be guarded against in every possible way. Fortunately the East coast of Africa is still free from the disease and great precautions are being taken to rid all airplanes operating in the African endemic areas of the disease of the mosquito carriers. For this purpose Dunnahoo advocates the use of the pyrethrum mixture known as the Freon bomb referred to above in the section on malaria. It is being increasingly recognized that monkeys often are carriers of the yellow fever virus. Thus, Kirk reports that in the area of the Nuba Mountains (Anglo-Egyptian Sudan) yellow fever epidemic of 1940 from 20 to 25 per cent of the monkeys have immune bodies against yellow fever in their blood which are due to earlier infection. Further, Hughes records that about 20 per cent of the ubiquitous East African grivet monkey, *Cercopithecus aethiops centralis*, show similar immunity to yellow fever, so that they probably form a link in the spread of yellow fever since mosquitoes become infected from them.

Vaccines

In view of the constant absence of typical cases of yellow fever in endemic areas the immunization of troops and others going to such areas is the only practicable method of avoiding infection. Recent work has thrown light on the duration of the immunity produced by such vaccines; it can be estimated by ascertaining the time during which immune bodies are demonstrable in the blood in adequate amounts. Soper reports that the immune period is very long after the use of the 17 D strain of modified yellow fever virus. Fox and Cabral found that the antibodies reached a peak in the blood of the inoculated in the first six weeks and then in four years gradually fell to a stable level after a distinct drop at the end of the first year. They concluded that the immunity produced is clearly satisfactory for at least four years and probably for much longer. In children it does not rise to so high a peak and tends to fall more rapidly, so it is fortunate that the disease is nearly always mild in them. The occurrence of jaundice, occasionally of a serious nature, many months after vaccination against the jungle type of yellow fever in Brazil, has led to important investigations which show that this complication can be avoided by using serum-free vaccines. Thus, in Brazil, Fox, Kossobudzki and da Cunha found the use of serum-free vaccines in 1 in 100 saline dilutions to be safe; Hargett and his colleagues found an aqueous-based vaccine of 17 D virus prepared from infected chick embryos to be as effective as other vaccines and not to produce jaundice.

TRYPANOSOMIASIS

Epidemiology

Because of the discovery of four cases of sleeping sickness in Bechuanaland, South Africa, in 1938 together with the reoccupation of this area by *Glossina*—which had disappeared after the rinderpest outbreak at the end of last century—a sleeping sickness survey has been carried out and is reported on by Macaulay. *G. morsitans* was most prevalent in the areas of the thickest jungle; these can be located by aerial photographs. A serious recrudescence of sleeping sickness was found in one area. The inhabitants of the infected villages should be transferred to areas free from tsetse fly and bush clearing should be carried out. It is also suggested that infected Ngamiland should be surrounded by a cattle-free zone, that all the cattle in the infected area should be inoculated against rinderpest and that disease should be introduced for the purpose of killing off the ungulates in the swamp area in order to reduce the food supply of the tsetse—a somewhat heroic procedure. Pigs have been found by van Hoof, Henrard and Peel to be important reservoirs of trypanosomes pathogenic to man. In spite of the fact that the trypanosomes are very rare in the blood of these animals, which remain symptomless for long periods, they still readily infect *Glossina*.

Clinical picture

McDermott and his colleagues have found experimentally that deficiency of vitamin B complex predisposes to an optic atrophy in rats which is due to the administration of trypanamide.

Treatment

Further trials of diamidines (see Medical Progress (Critical Survey section) 1944, p. 100) have been reported during the past year. In Uganda Lawson, after from two to three months' treatment with pentamidine in fifty-three cases, found forty-one patients to be clinically cured, three much improved, four improved and four to show no change or to be worse; one patient had died. The toxic effects of the drugs were mild and the blood and glands were rapidly sterilized by their use. In advanced cases of patients with over 80 cells per cubic centimetre of cerebrospinal fluid, the drug failed or was uncertain. From ten to twenty daily injections were given of 0.5 gramme to children of from six to ten years of age and 0.1 gramme to persons over eleven years. In Sierra Leone, Lourie found pentamidine when given in 0.1-gramme doses daily for twelve days to be equal in its effects to those of trypanamide in the treatment of early cases of sleeping sickness; in late cases the latter drug was much more effective. Stilbamidine was considerably less effective than was pentamidine.

TYPHUS FEVER

Distribution

No reliable information appears to be available regarding the recent incidence of louse-borne epidemic typhus fever on the continent of Europe. McConn has recorded that in West Galway in the autumn of 1942 several cases were reported and that eighty-nine of 110 persons with a history of recent illness gave positive Weil-Felix reactions. Moreover, head lice or body lice were found on over half the number of persons (535) investigated.

Diagnosis

Gaud reports favourably on the micro-reaction of Castañeda and Silva's method as modified by Brumpt. A drop of finger blood is mixed on a glass slide with a drop of a suspension of *Proteus OX 19*, stained with methylene blue and sterilized by formol, and the slide is kept moving by tilting it with a circular movement. In positive reactions the uniform greenish-brown colour is changed within from one or two to four minutes by its becoming surrounded by a blue ring of agglutinated stained bacilli. Agreement was found between the reaction to this test and the standard Weil-Felix reaction in 96 per cent of cases, and almost invariably in cases in which the Weil-Felix reaction titre was 1 in 200 or over. Another promising diagnostic method is the Giroud intradermal test which is reported on by Clavero and Pérez Gallardo. In this test suspensions of *Rickettsia prowazeki*, cultivated by Cox's method in the vitelline membranes of embryo chicks, are used. For the test 0.25 cubic centimetre of a suspension of the organism is mixed with an equal quantity of undiluted serum for from twenty to ninety minutes and is then injected into the shaved skin of white rabbits in dilutions of 1 in 10, 1 in 100, and 1 in 1,000; similar suspensions unmixed with serum are injected into control animals. The serums of forty convalescent typhus fever patients all gave reactions in the form of a central necrotic spot surrounded by nodulation and an outer zone of hyperaemia. In four cases of other diseases there was not any reaction so that the test may be of use in detecting 'inapparent' attacks of typhus fever and in estimating the protective value of vaccines or serums.

Vaccines

Tests of six varieties of typhus vaccines, together with controls, are recorded by Ding. There were striking results in the reduction of mortality among infected persons subsequent to the use of the vaccines but not in prevention of attacks of the fever. About an equal number were inoculated in both groups each of which appears to have included some 200 persons. The vaccines used included those of Weigl and Cox and Giroud's lung cultures. After the use of each of them there was either no death or one death as compared with a rate of 33.3 and 20 per cent respectively in two series of controls. The most commonly used Cox's vaccine of *R. prowazeki* showed neither complications nor deaths among the infected.

Prophylaxis

The delousing of persons exposed to infection with typhus fever remains the most effective preventive measure against epidemic typhus. In the United States Army (Article, *Soap*²) a powder, containing as its most active ingredient dichlorodiphenyl-trichlorethane, when used against lice as well as against bugs and other insects has been found to be much more effective for this purpose than was the old pyrethrum compound preparation. Mattresses treated with the new preparation are said to remain free from such insects for sixty days.

Serum treatment

Immune rabbit serum is favourably reported on in the treatment of Rocky Mountain tick-borne endemic typhus fever, by Topping. Rabbits can be immunized by the injection of virulent *Rickettsiae* obtained either from infected ticks or from yolk-sac cultures and the serums of the animals can be concentrated. Inoculated guinea-pigs can be saved by a dose of 0.5 cubic centimetre of purified rabbit serum given on the first day. The serum was tried in seventy-one cases of patients with Rocky Mountain spotted fever none of whom had been previously protectively inoculated. The full dose was about 1 cubic centimetre per kilogram of body weight. First, a dose of about

1 cubic centimetre was injected intramuscularly, then 5 cubic centimetres were given after ten minutes and the remainder of the full dose after a further ten minutes if a reaction did not occur. In fifty-two cases treated on or before the third day of the rash only two patients died; in nineteen cases treated later there were also two deaths—ten times less than the expectation based on ten years' experience. Further work on these lines is awaited with interest.

BACILLARY DYSENTERY

Polyneuritis

From the Russian front Wilke has reported a number of cases of polyneuritis which occurred after attacks of bacillary dysentery of a chronic type in which motor paralyses and sensory disturbances were prominent symptoms. Most of the patients had previously had Flexner or Shiga-Krause infections of the large bowel. Paralysis was noted chiefly in the proximal muscles combined with difficulty in walking or squatting or in stretching out the arms. Conjunctivitis and arthritis were often present as well. On the healing of the dysenteric lesions recovery of the nerve symptoms was usually remarkably rapid.

Sulphonamide treatment

Smyth and his colleagues report on the comparative value of sulphaguanidine and succinylsulphathiazole in the treatment of dysentery during an outbreak in a large institution which was traced to two *Bacterium flexneri* carriers who served food in a patients' kitchen. The first-mentioned drug was given in doses of 0.1 gramme increased to 0.3 gramme per kilo body weight daily in six equal parts and the second drug, in doses of 0.25 gramme per kilo body weight, was administered in a similar manner. The treatment was controlled by complete urine analyses made on alternate days. There were not any complications observed except slight sickness. Both drugs proved to be of value, but succinylsulphathiazole is considered to be the drug of choice in Flexner dysentery. Roberts and Daniels report on the use of succinylsulphathiazole during a dysentery outbreak in a camp for American soldiers. The outbreak was due to the Flexner group of dysentery bacilli with clinical signs which in part resembled those of acute food poisoning. The drug was given in eighty-nine cases and 136 men served as controls. The dosage was 0.25 gramme per kilo body weight at four-hourly intervals until the fever and diarrhoea had ceased for a period of two days. No significant differences in the duration of the diarrhoea and the amelioration of the symptoms were noted between the two series of cases. In the control group 18 per cent of the patients whose stools were originally positive became carriers after clinical recovery had taken place but only 2.6 per cent of the treated cases remained positive bacteriologically while they were being observed for an average of eighteen days subsequently.

Treatment by sulphonamides in diarrhoea and dysentery in children is reported on by Meyer who was working in Palestine. The cases were mostly in infants of from six to eight months of age, among whom before the use of the new drugs the mortality was 50 per cent in toxic cases. In a total of 344 cases 220 were treated with ultraseptyl (sodium sulphamethylthiazole); fifty-four received sulphaguanidine and seventy sulphapyridine, with a mortality of only 11.7 per cent in 196 toxic cases and only five deaths in the remaining 148 non-toxic ones. Sulphathiazole proved to be more effective in the toxic form of the disease probably owing to the fact that it is more readily absorbed. The drugs also showed an anti-diarrhoeal action unequalled by any previously used drug; in most cases the stools became formed and normal in three or four days. The doses were 0.1 gramme or less per kilo body weight daily for four or five days. Bograchow at the same hospital found that the summer peak mortality disappeared with the above treatment and that the deaths fell in the more serious toxic cases from 57.4 per cent in 1940 through 38.3 per cent in 1941 to only 13.9 per cent in 1942.

CHOLERA

Sulphonamide treatment

The *in vitro* effects of sulphonamides against *Vibrio cholerae* have been studied by Sadusk and Oswald. Care was taken to distinguish between the bacteriostatic and the bactericidal effects. Sulphathiazole showed great superiority in bacteriostatic action at 0.1 milligram per 100 cubic centimetres over sulphadiazine, sulphaguanidine and

sulphanilamide, but sulphaguanidine, on account of its less ready absorption from the bowel, may be preferable—with its use concentrations of over 200 milligrams per 100 cubic centimetres may be obtained in the stools. The action of aniline dyes upon cholera and other vibrios has been tested *in vitro* by Panja and Ghosh. Among twenty-two dyes examined the most effective were brilliant green or malachite green, crystal violet or methyl violet and gentian violet. Brilliant green in a dilution of 1 in 100,000 exerted a selective bactericidal effect on most Inaba and Ogawa sub-types of *V. cholerae* and on many paracholera vibrios isolated from clinical cases of cholera; it was harmless to non-agglutinating vibrios which were obtained from the Hoogly river water. Thirty-five cholera cases were treated with brilliant green without marked clinical improvement as a rule, but with earlier disappearance of vibrios from the stools than that which occurred in control cases.

AMOEBIASIS

An outbreak of amoebic infection of the bowel in a New Orleans children's home is reported by Ivanhoe. In 1939 the *Entamoeba histolytica* infection rate among 130 orphans up to the age of six years was found to be 84 per cent in spite of the fact that the home was very clean. Investigations revealed cysts on furniture, toys and other objects. Disinfection by means of steam and mass treatment removed both the *E. histolytica* and coincident helminthic infections in four weeks. *E. histolytica* have been demonstrated by Ott in the duodenal contents removed by a duodenal sound in six out of thirteen patients in whom amoebic infections of the large bowel had been found. Both cysts and free forms were met with but only one patient showed evidence of hepatitis.

Amoebic abscess of the liver

The treatment of this serious but now not very common disease is dealt with by Cameron and Lawler. They advocate the usual treatment by aspiration in combination with emetic treatment in all cases which do not show mixed infection, together with air replacement at the time of aspiration. Three radiographs were taken both before and after the operation—two in the erect position from in front and laterally and one with the patient lying on his left side—in order to determine the position, size and shape of the abscess cavity. A repetition of the X-ray examination a fortnight and more after the aspiration will allow the shrinkage of the abscess cavity to be watched; the air is not absorbed for a period of a month. Twelve cases have been successfully treated by the method.

LEPROSY

The control of leprosy

The Government of India Central Advisory Board of Health has issued a report, which was drawn up by a committee of experts, on leprosy and its control in India. After a historical introduction the advances during the last two or three decades in our knowledge of the subject are reviewed and the following main conclusions are reached. Great advances have resulted from improved treatment but the earlier hope that large-scale out-patient treatment at numerous clinics would solve the leprosy problem in India has not been fulfilled; the clinics however have much facilitated valuable surveys and epidemiological inquiries. Leper colonies for the isolation of the more infective cases are also required in every province, but as yet only Madras possesses one such institution. Home isolation too has been tried in villages, as was recommended by Muir, but it has not yet proved to be of much value. The leprosy research section of the Calcutta School of Tropical Medicine has done valuable work, but it is handicapped by not having any in-patients under its control. It is therefore suggested that a separate leprosy research institute should be provided in a large rural in-patient colony. A new and more comprehensive Leprosy Act is also suggested.

Nigeria, with more than five times as high a leprosy rate per thousand as India, has made more progress towards finding a solution of the problem. So far work has been carried out only on an insufficient—although expanding—scale, as recorded by Davey in his fourth annual report on Leprosy Control in the Owerri Province of Nigeria. A central leprosy colony together with forty-four out-patient clinics provides weekly treatment for 11,500 leprosy patients, most of the cases being of early amenable type.

In addition thirty-four model leper villages have been constructed on sites provided free of charge by native chiefs, with land to cultivate so that the villages can be self-supporting. Several hundred patients have been discharged recovered. A third survey made in one area showed only forty new cases—all of the earlier stages of the disease—to have occurred among 7,000 people. The highly infective cases were thus already isolated in the leper villages and so could not infect the healthy; there is good reason to expect a considerable decrease of the disease in areas in which such complete control has been obtained with the cordial cooperation of the people, who are clamouring for great extensions of the work among them. All this has been accomplished within a few years by two missionary doctors with the help of Toc H workers and an African staff trained at the headquarters of the leprosy colony at Uzuakoli. Similar work is being carried on at the Oji River and other such colonies but with an estimate of 200,000 or more leprosy cases in Nigeria only a beginning has been made to solve an urgent problem.

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PULMONARY TUBERCULOSIS

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The increased mortality from tuberculosis since the outbreak of the present war is a phenomenon which, in view of the experience of the war of 1914-18, can hardly be said to be unexpected, in fact it has been to a large extent anticipated by those chiefly concerned with the study of this disease. During the last quarter of a century our whole conception of human adult pulmonary tuberculosis has undergone a considerable change in comparison with that entertained for some years after Koch's epoch-making discovery and before what may perhaps be described as the foundation of the new pathogenesis for which much of the credit must be given to the work of Aschoff. Upon this basis have been built up the principles on which our present teaching in regard to phthisiogenesis may be said to rest, in the following of which our present elaborate and highly technical methods of treatment have gradually emerged. War has always been a great teacher in Medicine and although it would hardly be correct to say that the present struggle has actually revealed to us truths about pulmonary tuberculosis which were unknown prior to its outbreak it has provided us with opportunities for testing on a large scale the validity of many of the theories which we have developed in regard to the aetiology, the natural history and the prevention of the disease. It seems opportune at this moment to review some of the main features in our changing conceptions of the disease and to consider some of the problems in preventive medicine which have arisen in consequence of the formation of new ideas.

Many years ago Sir Robert Philip gave expression to the truth that the key to an understanding of the problem of adult pulmonary tuberculosis was to be found in a study of the disease in childhood. Much work has been done in the last two decades on the subject of infection in the early years of life and its relation to the development of active disease during adolescence or in the young adult period. The results of research into the tuberculin (Mantoux) reaction in children and into the natural history of the primary complex are by now well known to all serious students of tuberculosis and form what may be called the first chapter in our knowledge of the general lines on which successful prevention is likely to proceed. The work of Opie^{1,2}, Macphedran and others in the United States of America has been followed by observations of a similar kind in Great Britain, among which may be mentioned in particular the Prophit research (Ridehalgh) carried out under the auspices of the Royal College of Physicians, and the investigation of child contacts at the Brompton Hospital, where an extensive system for the purpose of watching progress has been built up thanks to numerous research grants from the Sir Halley Stewart Trust. It is to the work of the Halley Stewart Fellows at Brompton that credit is due for what may be fairly described as the first real experiment in mass radiography. This was one of the earliest instances of recognition of the value of radiology in the detection of pulmonary lesions in their minimal stage long before there had occurred in the lung structural damage of an extent sufficient to cause physical signs or symptoms such as ordinarily could be identified.

SYMPTOMLESS ADOLESCENT PULMONARY TUBERCULOSIS

In the latest publication from the research department of the Brompton Hospital (Macpherson) attention has been especially drawn to the S.A.P.T. class (symptomless adolescent pulmonary tuberculosis) for which in an increasing number of instances the induction of artificial pneumothorax has been advocated within a very short period after the recognition of the lesion. Such a line of approach has already given rise to criticism and to some controversy, and since it is perhaps somewhat revolutionary, at any rate in the minds of many people who are inclined to rely upon slower and more

conservative methods, it may be of advantage here to comment upon the reasons which have led to its adoption.

In the course of routine examination of large numbers of children who have been in contact with parents or other relatives who have attended the hospital with active pulmonary tuberculosis, a substantial proportion have been found to exhibit radiological evidence of minimal lesions of the lung, potentially tuberculous. Whereas many of these children, examined as they are at frequent intervals over a period of years, show satisfactory indication of their natural immunity by the appearance in later radiograms of unmistakable evidence of calcification of the original lesions, others are less fortunate: serial X-ray examination of the latter reveals changes in the extent and character of the shadows that leave no reasonable doubt about the presence within the lung parenchyma of a spreading granuloma. In some instances treatment by enforced rest results in retrogression of the disease with ultimate calcification, but in others the lesion continues to spread although constitutional disturbance may be absent and the child may not manifest any obvious signs or symptoms of serious illness. The decision to initiate collapse therapy has never in this department been made lightly or without due regard to all the relevant circumstances in each individual case, but the experience of the last few years has led to an increasing inclination to adopt this active method of treatment at an earlier stage than was formerly thought to be desirable. Especially is this so in the case of older children, that is in children who have reached the stage of early adolescence and have entered the age group which all recent statistics have shown to be the least favourable and most dangerous, particularly in females. It is chiefly owing to past experience of the failure of more conservative methods (often because, in the social section to which the patients under consideration belong, the obtaining of prolonged rest is impracticable) that time and again pneumothorax therapy has been undertaken at so early a stage of the disease. Knowledge of such failure and of the disastrous results which so often are obtained in these highly susceptible individuals is the justification for a trial at least of a more robust procedure the technique of which is the simpler the earlier it is begun and the complications of which are less likely to be encountered when the lung lesion is minimal and when the pleura has not yet become involved.

The silent lesion in pulmonary tuberculosis is no less a problem in the young adult than it is in the contact child and the use of mass radiography has provided striking examples of the fact within the last two or three years. Just how far the application of this latest advance in our knowledge of preventive methods can be made universal is still a matter for speculation. The introduction of miniature mass radiography for the ostensibly healthy among the industrial population has so far been accepted with intelligent interest and without as much prejudice or resentment as might have been anticipated. It is however obvious that an attempt to perpetuate it as an integral part of the future machinery of social medicine in Great Britain—and from a purely scientific standpoint this is surely the ideal policy—is bound to raise many difficulties, social, ethical, financial and so forth, which will carry the whole question into regions far beyond those so far envisaged by even the most ardent advocates of a national fluorographic service. Space does not permit of fuller discussion of this important problem but attention has been called here to this aspect of work in tuberculosis as one of the most stimulating of recent advances and one which is likely in the near future to make increasing calls upon the time and the consideration both of politicians and of the medical profession.

PRIMARY INFECTION AND SECONDARY LESIONS

From what has just been said it will be realized that one of the salient points in the problem of pulmonary tuberculosis is that of primary infection and its relation to the development of the secondary lesions which are directly responsible for the clinical manifestation of the disease when it occurs. I have referred to this as the keynote of what may be called the new pathogenesis—not indeed that it is so new, for the pathology of the primary complex has been known for many years. It is however only in comparatively recent times that the newer conception of endogenous reinfection has begun to receive general acceptance and to provide the rational basis for more adequate control of exudative pulmonary lesions in the earliest possible recognizable stage.

I have said that the present war has given us further opportunity for the realization

of these vital principles. In a recent article by Daley and Benjamin reference is made to the rate of occurrence of new cases of pulmonary tuberculosis in London; the rate is shown to have increased in the year 1941 as compared with the year 1938 by as much as 43 per cent. The general increase in tuberculosis appears to have affected children rather more than it has adults, especially as regards the non-pulmonary type, but the number of new cases of pulmonary tuberculosis increased more in adults than did the number of new cases of the non-pulmonary disease; from this fact the authors draw conclusions concerning the importance of contact infection and of droplet infection in London. Various factors operating in different directions have been taken into account and duly valued in this interesting statistical survey, but the effects of strain and overcrowding from bombing, which are among the more obvious factors, can hardly be overestimated. An even more trenchant comment on mass infection is contained in the war review of Heaf and Rusby who note the considerable amount of infection among the general population with which the children are coming in contact. In explanation of the increase in such mass infection by sputum-positive cases they point to the probable frequency of dangerous contact in the first half of the year 1941 during the nightly bombing of the large towns. These observations are of particular interest and importance in that they indicate the growing tendency to view with increasing seriousness the problem of contact infection in children and in adolescents. The doctrine of the hereditary aetiology of tuberculosis died hard, and even when the significance of sputum as the medium through which the seed is sown was realized by the medical profession we were still far from an adequate understanding of the pathology of the primary complex or from a full development of the conception of child tuberculosis as the keynote of adult disease, an enlightened view which the genius and vision of Sir Robert Philip enabled him to express long before the idea had been grasped by the majority of specialists in phthisiogenesis. That the size of the primary infecting dose is a matter of no little importance is now generally held to be at least one of the probable hypotheses, and the fact that so much work has been done in the last two or three years on the Mantoux test in children, with emphasis on the need for the special care and protection of the negative reactor, is evidence of a real advance along rational and scientific lines.

THORACIC SURGERY AND COLLAPSE THERAPY

Of recent advances in treatment perhaps the most significant is not only the improvement in the technique of thoracic surgery but also, even more important, the growth of a better understanding of what is implied by the term collapse therapy. In its most modern connotation this is taken to embrace all measures designed to immobilize a lung which is the seat of active disease and to obliterate cavities which form a main reservoir from which metastatic infection may reach other and healthy sites by way of the lymphatic glands and vessels and the blood stream. Thus artificial pneumothorax, diaphragmatic hemi-paralysis (temporary or permanent), pneumonolysis, and various degrees of thoracoplasty are all viewed as different tactical manifestations of one common strategy. That such a conception of team work be held by physicians in charge of the management of a phthisical patient is an ideal to which I believe we have approached much nearer in the last few years.

A few words may be said about tuberculous tracheo-bronchitis, not only because of its importance in enabling a better understanding of some of the symptomatology in chronic cases of pulmonary tuberculosis but also because of the bearing it has upon the subject of artificial pneumothorax therapy. Benedict has in a recent contribution drawn a clear and important distinction between three main forms of this condition which have come under his observation and has emphasized the need for bronchoscopic examination in addition to radiology in order to establish the diagnosis. His paper should be read as a preliminary to an understanding of the various other communications on this disease which deal particularly with the relation to treatment in the pulmonary form. The surgical aspects of the matter have been fully reviewed by Tudor Edwards. A more recent commentary has been published by Salkin, Cadden and Edson in which reference is made to the greater severity of the clinical course and to the less favourable prognosis in cases of tuberculosis of the lungs complicated by tuberculous bronchitis than in cases in which the bronchi were normal. The importance of this in treatment is emphasized by Rafferty and Shields who note that of the

two main operations of collapse therapy—artificial pneumothorax and thoracoplasty—the former interferes with bronchial drainage much more than does the latter, which may therefore be preferred to pneumothorax therapy in cases in which tuberculous bronchitis complicates the parenchymatous lesion and causes a certain degree of bronchial occlusion. The implications are obvious. So far-reaching are the results which their logical application would have upon our mode of treatment that even the most progressive may well feel at first a little dismayed at the prospect, but the views put forward by these authors are founded on careful observation and clear thinking and they cannot lightly be set aside.

PARATUBERCULOUS LESIONS

The relation between tuberculosis and erythema nodosum has always been a matter of interest to students of immunology and a review of the year's work on pulmonary tuberculosis would be incomplete without reference to some recent observations by Kerley^{1,2} on the radiological manifestations of erythema nodosum, a condition classed by Collis in 1932 among the so-called paratuberculous lesions. Kerley's series comprises some fifty cases in which serial radiograms and tomograms showed gross changes within the thorax, the most obvious of which were massive enlargements of the bronchial glands with or without changes in the lung parenchyma in the form of reticulation or of miliary nodulation. Emphasis is laid on the importance of marked enlargement of the root glands as a salient feature of Besnier-Boeck-Schaumann disease and, although admitting that both tuberculosis and streptococcal infection must be included as possible aetiological factors, Kerley maintains that a relationship with sarcoidosis although not proven is much more probable. His contention is supported by clear and convincing arguments reinforced by the evidence supplied by excellent reproductions of typical radiograms.

CONCLUSION

It remains, in conclusion, to attempt some estimate of the general trend of thought in regard to pulmonary tuberculosis, its pathogenesis, its behaviour, its treatment, the general outlook in prognosis in individual cases, and the possibilities that lie before us in respect of the control and prevention of this national scourge. Looking back upon the history of the gradual evolution of our knowledge of the effects upon the human body of Koch's bacillus, I incline more and more to the view that further progress in the control of the disease will depend upon study of the soil rather than upon study of the seed. A better understanding of the problem of how best to combat the increase in incidence with which we shall undoubtedly be faced in the years succeeding the cessation of hostilities in Europe must be based on a conception of pulmonary tuberculosis as not so much a disease of the lungs as a general infection with a local manifestation, the delicate and highly vulnerable lung parenchyma being an easy target for attack. The exacerbation of active disease in the lung which so often is evident after a normal confinement in a young tuberculous woman is a phenomenon as striking as the relative immunity and apparent healthiness usually observed in her in the preceding months of pregnancy. Here is food for thought which may well be assimilated by those whose studies lie in the field of biochemistry. The elaborate changes that occur in the human body at the different epochs of its existence are as yet but little understood. It would seem an obvious hypothesis that during pregnancy there are manufactured protective substances designed by Nature for her supreme object, the propagation of the race; these may include substances which inhibit the activity of the tubercle bacillus and delay the inevitable progression of the pulmonary lesion until the time when Nature's aim is achieved in the birth of the future man or woman. Then in the succeeding biochemical cataclysm the protecting substances are removed and we witness the sudden and dramatic clinical spread which heralds the progressive downhill course of the patient. It is more than possible that in this direction we may one day find the beginning of some new discovery which may form the basis of a treatment of this dread disease on logical and rational lines.

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RECENT DEVELOPMENTS IN
DRUG THERAPY

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SIXTH ADDENDUM TO THE BRITISH PHARMACOPOEIA 1932

The Sixth Addendum to the British Pharmacopoeia 1932 came into official use on 1st August 1943. In it recognition is given to a number of important drugs, and some of the amendments are of significance to the practitioner.

Names recently approved

Acetomenaphthone.—1 : 4-diacetoxy-2-methylnaphthalene. Acetomenaphthone is a white crystalline powder which is either odourless or smells faintly of acetic acid; it is almost insoluble in water. Dose: from 0.01 to 0.06 gramme. Acetomenaphthone (see Medical Progress (Drugs section) 1943, p. 94) has the advantage over menaphthone (vitamin K) in that it is readily absorbed from the intestine. It is given, in tablet form, for the purpose of restoring the prothrombin content of the blood to the normal within from twenty-four to forty-eight hours; thus it accelerates the delayed coagulation time which occurs in sprue and prevents post-operative haemorrhage in obstructive jaundice. Acetomenaphthone is also valuable when given to the mother during a week before labour, or to the infant in doses of from 5 to 10 milligrams, for the prevention and treatment of infantile haemorrhagic diathesis due to the fall in the prothrombin level during the first week of life. It is not of any value in a recurring haemorrhage which is not due to lack of prothrombin.

Acidum ricinoleicum.—This mixture of fatty acids which is obtained by the hydrolysis of castor oil is a yellowish-brown oily liquid which increases the bactericidal action of chlorinated phenols in soap solutions and is, therefore, a constituent of liquor chloroxylenolis. Sodium ricinoleate solutions (1 to 4 per cent) are antiseptics and, since they lower surface tension, penetrate and cleanse pyorrhoeal pockets effectively; it is doubtful whether or not the drug has an inhibitory action on the organisms which cause gingivitis and pyorrhoea alveolaris. Tooth-pastes containing this soap can be purchased.

Alcoholia lanæ.—Wool alcohols, which are the fraction, containing cholesterol (28 per cent) and other alcohols, obtained by the saponification of the grease of sheep's wool, form a golden-brown solid which is plastic when warm, and melts at 54° C. Wool alcohols make good water-in-oil emulsions which are absorbed by the skin. They are used, combined with hard, soft and liquid paraffin, in unguentum alcoholia lanæ as an ointment basis and as emollients and protectives for the skin.

Chloroxylenol.—*Parachlorometaxylenol*. 2-chloro-5-hydroxyl-1 : 3-dimethylbenzene. Chloroxylenol is almost insoluble (1 : 3,000) in water but is readily soluble in alkali hydroxides. It is used in the form of liquor chloroxylenolis (roxenol), a yellow soapy liquid, which contains chloroxylenol 5 per cent and terpineol 10 per cent with ricinoleic acid 5 per cent, alcohol, and solution of sodium hydroxide in distilled water. This is not irritant to the tissues, has a low toxicity, and is used as an antiseptic for wounds (1 in 100 of water), for gynaecological and obstetrical purposes (1 in 50 of water) and as a gargle (from 1 in 200 to 1 in 500 of water).

Dithranol.—1 : 8-dihydroxyanthranol. This is a yellow odourless and tasteless powder used as unguentum dithranolis, 0.1 per cent in yellow paraffin, in the treatment of psoriasis, chronic eczema and lichen planus.

Injectio procainæ et adrenalinae (4th Addendum).—This solution, which contains 2 per cent of procaine hydrochloride, is changed in title to *injectio procainæ et adrenalinae fortis*.

Injectio procainæ et adrenalinae mitis.—A new weak injection of procaine and adrenaline is introduced with this title, and is made as follows. Mix, immediately before it is to be used, a sterile solution of procaine hydrochloride—consisting of procaine

hydrochloride 2, sodium chloride 0·8, chlorocresol 0·1 in distilled water 100—with 3 times its volume of physiological solution of sodium chloride for injections, and add solution of adrenaline hydrochloride in the proportion of 0·2 cubic centimetre to each 100 cubic centimetres of the procaine hydrochloride solution. Dose: for infiltration anaesthesia, up to 300 cubic centimetres (up to 10½ fluid ounces).

Kaolinum.—The title of kaolin is altered to that of *kaolinum ponderosum*. It is used in making cataplasma kaolini composita, and a new light kaolin, *kaolinum leve*, is introduced and shall be dispensed or supplied when kaolinum or kaolin is prescribed or demanded. Kaolinum leve is intended for oral administration as an intestinal protective and adsorbent of bacteria and toxins; suspended in water it has been used with success as an adjuvant in the treatment of cholera, ulcerative colitis, bacillary dysentery and persistent diarrhoea. Dose: from 15 to 60 grammes (½ to 2 ounces).

Menaphthonom.—2-methyl-1 : 4-naphthaquinone (menadione). This yellow crystalline powder is insoluble in water, and has the action and uses of vitamin K (see Medical Progress (Drugs section) 1943, p. 94) in increasing the prothrombin content of the blood when it is deficient, for example in neonatal haemorrhage or in obstructive jaundice. It is given by intramuscular injection in 0·5 per cent solution in sterilized arachis oil and acetomenaphthone may be given orally afterwards. Dose: by intramuscular injection, from 0·005 to 0·01 gramme.

Nicotinamide.—Nicotinic acid amide (pyridine-3-carboxylic acid amide). This crystalline powder with a bitter taste has the actions and uses of nicotinic acid in the prevention and treatment of pellagra. Its advantages are (1) that it does not produce itching of the erythematous patches or the facial flushing and faintness which nicotinic acid may cause and (2) that it is more suitable for administration by injection. Dose: from 0·02 to 0·1 gramme. Cases of acute nicotinic acid deficiency have recently been described and treated (Gottlieb). Addition of nicotinamide to the diet of fit young men produced, in the course of experimental tests, increased muscular effort and coordination (Frankau).

Riboflavina.—Riboflavine. 6 : 7 - dimethyl - 9 - (*d* - 1' - ribityl) - isoalloxazine (lactoflavine). Dose: from 0·001 to 0·01 gramme. This is an orange-yellow crystalline powder, slightly soluble in water. Riboflavine (vitamin B₂), when its phosphoric acid ester is conjugated with certain proteins, constitutes flavo-protein enzymes, which are essential factors for the tissue oxidation of aldehydes, carbohydrates, lactic acid and amino-acids. The daily adult requirement is about 1–3 milligrams. Riboflavine is absorbed by the alimentary tract; it is absorbed to a less extent when there is achlorhydria or diarrhoea; any surplus is excreted by the kidney as uroflavine.

Ariboflavinosis was described by Sebrell and Butler in 1938 and subsequent reports have extended although not completely clarified our knowledge of this symptom-complex. Ariboflavinosis is characterized by a combination of oral, skin and ocular lesions. Bilateral transverse fissures (cheilosis, *perlèche*) appear at the angles of the lips, which are red and shiny; the tongue is purplish or magenta-red and is fissured, and its papillae are flattened or mushroom shaped. A scaly, greasy or seborrhoeic desquamation gives rise to crusts at the edges of the lips, naso-labial folds and eyelids and on the ears. The ocular symptoms are photophobia, impaired vision in dim light, itching or burning of the eyes and lacrimation; examination shows the presence of bilateral dilatation of the sclerotic vessels and circumcorneal injection due to capillary invasion from the limbic plexus of the cornea (corneal vascularization) (Gregory). The claim that rosacea keratitis is due to ariboflavinosis is not confirmed by Fish. None of these symptoms individually can be regarded as specifically due to ariboflavinosis but a combination of the lesions does respond to riboflavine treatment.

Administration of riboflavine has produced improvement in the dermatoses of pellagra, acne rosacea, rosacea keratitis, corneal ulcer and interstitial keratitis. It has also been stated that the giving of it cures interstitial keratitis due to hereditary syphilis (Corner). A final assessment of the symptoms caused by its deficiency and of its therapeutic applications cannot be made with reliability at present (Cosgrove; Scarborough; Sydenstricker, Sebrell, Cleckley and Kruse; Tisdall, McCreary and Pearce).

Stilboestrol.—Diethylstilboestrol. 4 : 4' - dihydroxy - α : β - diethyl - stilbene. Stilboestrol is a crystalline powder which is very slightly soluble in water but which dissolves in aqueous solutions of alkali hydroxides. Dose: from 0·0005 to 0·002 gramme. The uses of stilboestrol were described in Medical Progress (Drugs section) 1943, p. 98. It has recently been proved to be successful in the treatment of prostatic carcinoma.

The proof rests upon two facts: (1) prostatic carcinomas, which have a high acid phosphatase content, consist not of embryonic cells but of normal epithelial cells in which malignancy has developed; (2) this tissue can be made to atrophy if the androgenic hormones are reduced either (a) by castration or (b) by oral administration of oestrogens such as stilboestrol or (c) by hypodermic injection of oestradiol dipropionate. Stilboestrol and hexoestrol are readily absorbed when given orally; from 3 to 5 milligrams daily are given at first and the dose is reduced as the acid serum phosphatase falls to the normal and symptomatic improvement occurs; the control dosage may be 1 milligram or less daily. Successful results have also been reported from the use of oestradiol benzoate, which seemed to be better than the use of stilboestrol, given intramuscularly (Huggins and Clark; Herbst; Chute, Willetts and Gens; Kahle, Ogden and Gelzoff; Duncan).

Terpineol.—This is a mixture of isomers consisting largely of *dl*- α -terpineol and is a colourless, neutral, viscous liquid with a pleasant odour; it is insoluble in water. Terpineol is contained in liquor chloroxylenolis in which it acts as an adjuvant aromatic antiseptic.

Important alterations in composition and dose

Ergota praeparata.—This preparation is now standardized to contain 0.2 per cent of total alkaloids of ergot, calculated as ergotoxine, of which not less than 15 per cent consists of water-soluble alkaloids of ergot, calculated as ergometrine; or, with reference to the dose, 0.5 gramme contains 0.001 gramme of the total alkaloids, calculated as ergotoxine, and 0.00015 gramme of the water-soluble alkaloids of ergot, calculated as ergometrine. The dose is altered to from 0.15 to 0.5 gramme.

Pamaquin.—The dose is altered to from 0.025 to 0.05 gramme.

Paraffinum molle album.—Yellow soft paraffin (*paraffinum molle flavum*) may be substituted for white soft paraffin in prescriptions and in pharmacopoeial preparations.

Syrupus ferri phosphatis cum strychnina.—Easton's Syrup without quinine. Dose: from 2 to 4 cubic centimetres (30 to 60 minims). This preparation contains in 4 cubic centimetres (60 minims) 0.072 gramme of anhydrous ferrous phosphate, or about 0.034 gramme of iron, and 0.0012 gramme of strychnine hydrochloride. It shall be dispensed or supplied when *syrupus ferri phosphatis cum quina et strychnina* (Easton's Syrup) is prescribed or demanded.

Unguenta.—Unguentum aquosum (hydrous ointment) is the amended basis for the following unguenta: *acidi borici*, *acidi salicylici*, *hydrargyri ammoniati*, *hydrargyri oleati*, *hydrargyri subchloridi*, *sulphuris* and *zinci oxidi*. Unguentum *acidi tannici* and unguentum *hamamelidis* have a basis of distilled water and ointment of wool alcohols. Unguentum *hydrargyri* contains mercury 30 per cent, oleated mercury 1.5 per cent, in wool fat, white beeswax and white soft paraffin; unguentum *zinci oleatis* is made with distilled water and hydrous ointment; unguentum *zinci oxidi anhydrosus* consists of zinc oxide 15 in simple ointment 25.

BRITISH PHARMACEUTICAL CODEX

The Sixth Supplement to the British Pharmaceutical Codex, which was published in January 1944, establishes standards for non-sterile and for sterilized surgical catgut, amends the required standards for batiste, jaconet and oiled artificial silk, and gives additional amendments to the British Pharmaceutical Formulary.

THE SULPHONAMIDES

The clinical value of sulphonamide therapy both in surgery and in Medicine has been fully described in the Medical Research Council's *War Memorandum No. 10*, 'The Medical Uses of Sulphonamides'; this should be consulted. Reference is made here to information which has become available since the last summary was published in Medical Progress (Drugs section) 1944, p. 111.

Sulphapyridine

Sulphapyridine can be absorbed from the pleural cavity when it is introduced as a powder after operation, but its absorption is irregular and below therapeutic levels (maximum, 5.5 milligrams per cent); the average time for complete excretion is six days (Vickers). The value of sulphapyridine in clearing up Sonne dysentery infections

in five days has been confirmed; normal defaecation was restored in nine days (Swyer). Oral administration of sulphapyridine, sulphathiazole, sulphamezathine and sulphadiazine produced clinical cure of ophthalmia neonatorum usually in from three to eight days; gonococcal infections responded more rapidly than did the non-gonococcal cases. Dosage was uniform; no differences were observed in the effect of the four drugs but sulphadiazine and sulphamezathine were the most easily tolerated by the patients (Sorsby and Hoffa).

Sulphamethylpyrimidines

There is an unfortunate liability to confusion with the names and contractions for these compounds. Sulphamonomethylpyrimidine (sulphamerazine, sulphamerizine, S.M.) is monomethyl-sulphadiazine; and sulphadimethylpyrimidine (sulphamezathine, sulphamethazine, S.M.Z.) is dimethyl-sulphadiazine. Both compounds are absorbed rapidly from the intestine but are excreted slowly and, therefore, a high concentration in the blood can be maintained by giving doses less frequently. The acetyl derivatives of both compounds are more soluble than is acetyl-sulphadiazine but nevertheless renal complications have occurred from their use. If 3.5 grammes of sulphamonomethylpyrimidine (sulphamerazine) are given orally, the blood concentration in two hours is 8 milligrams, in four hours 10 milligrams and in twenty-four hours 6 milligrams per cent; the initial dose is 3 or 4 grammes orally (or given as the sodium salt intravenously) followed by 1 gramme orally every six or eight hours for ten days. The therapeutic value of sulphamonomethylpyrimidine in lobar pneumonia, cerebrospinal fever and other susceptible infections is comparable with that of sulphadiazine, and toxic effects, similar to those caused by the latter, have been observed (Melton; Hall and Spink; Hageman, Harford, Sobin and Ahrens; Murphy, Clark and Flippin; Welch, Mattis, Latven, Benson and Shields).

Sulphadimethylpyrimidine (sulphamezathine) is at least as effective as sulphapyridine in lobar pneumonia and it is also less liable to cause vomiting or other toxic effects; adults should receive 4 grammes initially by the mouth and 2 grammes at six-hourly intervals thereafter (see Medical Progress (Drugs section) 1944, p. 114; Macartney, Luxton, Smith, Ramsay and Goldman; Melton; Peters and Easby).

Sulphaguanidine

Clinical comparison shows that sulphaguanidine, when used in acute, subacute and chronic bacillary dysentery, is almost non-toxic and reduces the length of hospital treatment by half; sulphapyridine is less effective and causes nausea; sulphanilamide has not proved to be valuable (Bulmer and Priest). Flexner dysentery carriers were also successfully treated, although the development of toxic rashes was common (Smith). The fact that a chronic paratyphoid B carrier was successfully cured by administration of sulphaguanidine in three courses of seven days' treatment each, given at intervals of about six weeks, is of importance in preventive medicine (Loewenthal and Corfield).

Succinylsulphathiazole (sulphasuxidine)

This sulphonamide is only very slightly (5 per cent) absorbed; doses of 60 grammes given daily by the mouth are said to remove from the faeces all organisms except faecal streptococci. Succinylsulphathiazole has proved to be valuable in treating bacillary dysentery even when sulphaguanidine has failed (Caldwell and Hardwick), and also in the prevention of sepsis after abdominal gunshot wounds and colonic operations. Although succinylsulphathiazole breaks down into sulphathiazole in the presence of plasma and wound fluids, its decomposition rate is so slow that sulphathiazole is not absorbed in toxic amounts from large burns or wounds or from the peritoneum. Succinylsulphathiazole 20 per cent in a lanolin cream, locally applied, controls wound infections by Gram positive organisms but is not suitable for intraperitoneal use (Pulvertaft and Mackenzie).

PENICILLIN AND ITS DERIVATIVES

Penicillin is recognized to be a powerful bacteriostatic agent which can inhibit the growth of sensitive organisms in dilutions of 1 : 50,000,000; as it has a low toxicity (1 : 100 strength) towards leucocytes, their power as phagocytes is increased. The activity of penicillin is not reduced by serum, pus or tissue autolysates. The present measure of its activity and dosage is the Oxford unit, which is based on the bacterio-

static power of an arbitrary amount of a standard product. Penicillin is absorbed from the small intestine but cannot be given effectively by the mouth, because it is decomposed by gastric acidity, nor should it be given by the rectum. When it is injected subcutaneously or intramuscularly it is absorbed rapidly but it is quickly excreted in the urine; frequent doses are therefore required in order to maintain an adequate concentration in the blood. It is also excreted in the saliva and bile but it does not penetrate the cerebrospinal fluid; intrathecal injections of penicillin solutions are, however, safe and effective (Florey). The Gram positive organisms most sensitive to penicillin are *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pneumococcus*, *Gonococcus*, *Meningococcus*, *Bacillus anthracis*, *Clostridium welchii*, *Clostridium oedematiens*, *Corynebacterium diphtheriae* and some strains of *Streptococcus viridans* and *Actinomyces*. More or less resistant organisms are all Gram negative bacilli—the typhoid-dysentery group and coliforms generally, *Proteus*, *Pseudomonas pyocyanea* (*aeruginosa*), *Haemophilus* and *Brucella*, *Streptococcus faecalis* and *Mycobacterium tuberculosis*. Penicillin loses potency according to the length of time it is kept before use and phials should bear a label indicating the last date on which their contents should be used. Penicillin should be stored in a refrigerator.

Clinical experience and results with penicillin, calcium penicillin and sodium penicillin have been described very fully since the summary was published in Medical Progress (Drugs section) 1944, p. 115, by Fleming and Florey, by Florey and Cairns in a War Office Report on its use in war wounds in the North African campaign and recently in a report to the Medical Research Council on the work of a penicillin research unit at St. Bartholomew's Hospital (Christie and Garrod). These should be consulted for full details of experimental work, dosages, modes of administration and clinical results.

Use in war wounds

A comparison has been made of the merits of systemic administration of penicillin by (1) continuous intravenous drip transfusion (30,000 units of sodium penicillin in one pint of 4 per cent dextrose in 0.18 per cent saline, given in six hours), which gave a continuous and adequate blood titre but caused frequent and painful thrombophlebitis; (2) intermittent intramuscular injection (15,000 units given every three hours), which, although simple to perform, caused pain, disturbance of the patient and a variable blood titre; (3) continuous intramuscular drip infusion (two pints of intravenous solution in twenty-four hours), which, although it was painless and gave a continuously adequate blood titre, induced a tendency to local abscess formation (Morgan, Christie and Roxburgh).

In the treatment of war wounds, calcium penicillin (1 gramme = 50,000 units) is employed locally and sodium penicillin is administered by intramuscular or intravenous injection. Calcium penicillin is applied on wounds either (1) in solution (250 units per cubic centimetre of distilled water) or (2) as a powder (500, 2,000 or 5,000 units per gramme, diluted with sulphanilamide) or (3) as a cream (250 units per gramme in a lanette wax basis). Sodium penicillin solution (5,000 units per cubic centimetre) is injected intramuscularly for systemic treatment in doses of 3 cubic centimetres every third or fourth hour, but as these injections cause pain, an intravenous drip of sodium penicillin (100,000 units in 2 litres of glucose-saline) given during twelve or twenty-four hours is to be preferred; a continuous intramuscular drip infusion has also been recommended.

Owing to the small amounts of penicillin available, emphasis is laid on the necessity for confining the use of it to wounds infected with organisms known to be susceptible to the action of the drug. It has been found that speedy application is of importance, and early insufflation of the wound with penicillin-sulphanilamide powder is advocated; septic soft-tissue wounds can be closed after the insertion of $\frac{1}{4}$ -inch rubber tubes to allow for the injection of from 3 to 10 cubic centimetres of penicillin solution (250 units per cubic centimetre) twice daily for four days; in clean cases wounds may be closed after insufflation of powder only; it is recommended that wound excision, especially of skin, should be conservative. Wounds so treated remained dry or discharged a thin salmon-pink pus, which turned green on the dressing and was Gram negative pus containing *Ps. pyocyanea*. Compound, mostly comminuted, fractures, sustained from five to fourteen days previously, were treated locally in order to convert them to simple fractures by closure, and systemically by giving from 100,000 to

120,000 units daily by the three-hourly intramuscular route or by the continuous intravenous route over a period of from seven to ten days. In gas gangrene cases it is advisable to give systemic doses, to excise dead tissue and to administer antitoxin for the toxæmia; local application of penicillin is regarded as useless in treatment. In cases of infected brain wounds, pus was aspirated and the solution injected daily for from three to six days with favourable results. Burns were treated by insufflation with 1 per cent penicillin in sulphanilamide powder. It should be assumed that for each case 50,000 units of calcium penicillin for local application and 750,000 units of sodium penicillin for injection may be required (Florey and Cairns).

Penicillin applied every twenty-four hours as a cream (100 units per gramme) with lanette wax and soft paraffin is the most effective and economical way of treating burns and surface wounds; this removed Gram positive cocci from infected raw surfaces in from four to six days. When dry conditions are desired, penicillin-sulphanilamide powder is suitable; penicillin up to 20 units per square centimetre has not any adverse effects on skin grafts and its use facilitates grafting of raw surfaces (Bodenham).

General use

Penicillin in the form of drops (500 units per cubic centimetre) is easier to apply to the eye than in the form of an ointment and is effective against *Staph. aureus* and against haemolytic-streptococcal, pneumococcal and gonococcal infections. Applications should be at half-hourly intervals during the first twenty-four hours. Cases of acute conjunctivitis, blepharitis, corneal ulcer, perforating injury and dacryocystitis have been treated with success (Cashell).

In mandibular infections, chiefly osteomyelitis, after surgical removal of sequestra and closure of the wound, local treatment with 1,000 units of penicillin in 1 cubic centimetre was given through small-bore tubes every twenty-four hours. This eliminated all penicillin-sensitive organisms and gave satisfactory soft-tissue healing and bone regeneration; the average recovery time from this formerly very chronic condition was thirty days (Mowlem).

Early acute haematogenous osteomyelitis responds well to penicillin, but long-standing sepsis involving bone is considered unlikely to improve on either local or systemic treatment (Robertson).

Treatment of various soft-tissue lesions by penicillin cream (400 units per gramme) and of abscess cavities and cellulitis by a solution (1,000 units per cubic centimetre) indicated that early treatment, effective contact between penicillin and the infected tissue and removal of necrosed tissue are important factors in achieving sterilization by penicillin (Barron and Mansfield). The aspiration of breast abscesses (*Staph. aureus*) and the injection of from 2,000 to 20,000 units of calcium penicillin (2,000 units per cubic centimetre of distilled water), gave satisfactory results (Fraser). In diseases of the skin, calcium or sodium penicillin was applied as an ointment (400 units per gramme in a basis of equal parts of lanette wax, petroleum jelly and water). The drug is of obvious value in sycosis barbae, impetigo and blepharitis, and is effective in some cases of chronic eczema with secondary infection and of otitis externa (Roxburgh, Christie and Roxburgh). In acute pyogenic infections of the hand, the wounds at the operation were powdered evenly with calcium penicillin and packed with gauze soaked in penicillin paste (lanette wax 12, arachis oil 25, water 55) containing 150 or 250 units per cubic centimetre; the wound was covered with fine-mesh soft paraffin gauze in order to prevent the drug soaking out. Penicillin-treated cases—given adequate access and removal of dead tissue—were free from sepsis within a week; pus was scanty, and the relief of pain and throbbing, together with a rapid return of mobility, was striking except when tendon sheaths were involved (Florey and Williams).

Successful treatment by penicillin of a sulphonamide-fast streptococcal meningitis is reported as the result of eleven consecutive daily intramuscular injections of from 90,000 to 240,000 units, together with four concurrent daily intrathecal injections of 5,000 units. The bacteriostatic power of the cerebrospinal fluid was very strong twenty-four hours after the intrathecal injections had been made but it had disappeared at the end of four days. Since penicillin does not enter the cerebrospinal fluid from the blood, this case, like other cases of meningitis, might have responded to intrathecal administration alone (Fleming).

The American National Research Council's report on the use of penicillin has shown its value in various infections. The drug was given intravenously, intramuscularly and

by local injections. For intravenous administration a continuous drip of penicillin in 5 per cent glucose-saline was given at the rate of from 5,000 to 10,000 Oxford units per hour; intramuscular injections of 5,000 units per cubic centimetre were given at intervals of two or three hours. Rapid and successful results were obtained in cases of staphylococcal osteomyelitis, empyema, pneumococcal pneumonia and sulphonamide-resistant streptococcal infections; cure of sulphonamide-resistant gonorrhoea was also achieved in from nine to forty-eight hours by doses of from 100,000 to 160,000 units. Less striking results recorded in staphylococcal septicaemia and endocarditis may have been due to delay in treatment and to inadequate dosage (Keefer, Blake, Marshall, Lockwood and Wood).

Penicillin is probably the most effective drug for the treatment of gonorrhoea; sixteen doses of 10,000 units administered intramuscularly at three-hourly intervals cured seventy-two out of seventy-five cases of sulphonamide-resistant gonorrhoea (Mahoney, Ferguson, Buchholtz and van Slyke); twelve intramuscular doses each of 15,000 units given within forty-eight hours are also recommended (Florey and Cairns).

Sodium penicillin, 20,000 units given intramuscularly every three hours, has been successfully used in the treatment of cases of staphylococcal broncho-pneumonia and empyemas which were resistant to sulphonamides. The empyemas were treated by aspiration and by injection into the cavity of 20,000 units of calcium penicillin in 5 cubic centimetres of saline solution in the case of a ten-month-old baby; 60,000 units of sodium penicillin were used for an adult. As it is non-irritant to the pleura, penicillin appears likely to be a valuable drug in the treatment of empyema (Bennett and Parkes).

Inadequate supplies of penicillin have led to the making of home-made penicillin dressings and to accounts of successful results with them; their use is not to be recommended unless they are prepared under expert supervision (Hobson and Galloway; Annotation, *Lancet*; Article, *Pharmaceutical Journal*).

Patulin

This is derived from *penicillium patulum* and is anhydro-3-hydroxymethylene-tetra hydro- γ -pyrone-2-carboxylic acid. Pure patulin forms colourless prisms or plates which are soluble in water and have a neutral reaction. It is almost equally bacteriostatic to Gram positive as to Gram negative organisms (for example *Staph. aureus* in 1 : 60,000 solutions) but phagocytosis is inhibited by 1 : 2,000 solutions. As a nasal douche or spray it was found to relieve nasal catarrh; a solution in a phosphate buffer solution, adjusted to a hydrogen ion concentration of 6, was used in strengths of from 1 : 10,000 to 1 : 5,000 at two-hourly or four-hourly intervals in an extended trial for the treatment of the common cold; results were encouraging and there were not any ill effects; there is however no proof of any specific action. Patulin appears to be too toxic in action for use as an intravenous injection (Raistrick; Gye; Hopkins).

Claviformin, from *Penicillium claviforme*, is identical with patulin. The bactericidal action is due to combination with a protoplasmic constituent in cells; its activity is reduced in serum, and it is toxic to leucocytes in smaller concentrations than those which are required for the inhibition of bacterial growth (Chain, Florey and Jennings).

OTHER DRUGS

Thiourea and thiouracil

Thiourea (dose: orally per day, from 1 to 2 grammes) has a nauseous taste, gives the breath an unpleasant sweet smell and may cause vomiting even if taken in gelatin capsules. Thiouracil (dose: orally per day, from 0.2 to 0.6 gramme) is much more pleasant to take and is more acceptable by patients. Experimental evidence indicates that these drugs prevent the synthesis of the thyroid hormone either by hindering the iodization of tyrosine or by preventing the conjugation by oxidation of two molecules of diiodotyrosine to produce thyroxine. Both drugs, after an interval of about ten days, begin to relieve the tremors, nervousness and conspicuous ocular proptosis of thyrotoxicosis, decrease the size of the thyroid gland, lower the metabolic rate and increase the body weight. After three weeks' treatment, the dosage of thiouracil should be reduced to 0.2 gramme daily; a maintenance dose is established by its effect on the pulse rate, weight curve and metabolic rate, but leucocyte counts should be made each week. Toxic effects in the form of skin rashes and agranulocytosis have been recorded (Newcomb and Deane). Further experience with thiouracil will be necessary before a decision can be made whether it can control thyrotoxicosis or whether it is to be used

as a preparatory measure before operative treatment is undertaken (Astwood^{1,2}; Williams and Bissell; Himsworth).

Phenothiazine and gentian violet

The recommendation to use phenothiazine for the eradication of thread-worms (Manson-Bahr) has led to several reports that it produces toxic reactions, including severe haemolytic anaemia, particularly in children (Hubble; Johnstone; Bercovitz, Page and de Beer).

Gentian violet has proved to be highly successful in clinical use and has caused no more serious effects than vomiting when it has been used to remove thread-worms from children and from adults; purgatives are not required but an enema should be given for the purpose of emptying the lower bowel. Adults should be given 0.06 gramme as two $\frac{1}{2}$ -grain enteric-coated tablets or in gelatin capsules thrice daily after meals; children should receive 0.001 gramme per day for each apparent year of age, divided into three doses. Treatment is continued for five or seven days, an interval is allowed for a week, and a second course, if necessary, is then given (Wright and Brady; Cram).

Pethidine hydrochloride

The analgesic and antispasmodic properties of pethidine hydrochloride (dolantin, dolantal, demerol) have been stated in Medical Progress (Drugs section) 1944, p. 110. More recent experiences are recorded by Christie, and in neurological cases by Fitzgerald and McArdle. The drug has been used as an analgesic in obstetrics by the administration of either 100 milligrams intramuscularly, repeated after an hour, or of 100 milligrams intravenously followed after an hour by the giving of 100 milligrams intramuscularly, with or without hyoscine (scopolamine) $\frac{1}{160}$ grain; the combinations give an effective obstetric analgesia and pethidine has an antispasmodic action on the cervix. Pethidine produces analgesia within five or ten minutes after intravenous injection and within fifteen minutes after intramuscular injection. Unpleasant but not alarming maternal reactions were vomiting, dizziness, tingling of the limbs and dry throat (Gallen and Prescott; Spitzer).

Methedrine

This is *d*-desoxyephedrine or *d*-N-methylamphetamine hydrochloride (pervitin). Dose: from 0.003 to 0.006 gramme. Methedrine acts like its relatives ephedrine and amphetamine as a stimulant (sympathomimetic) of sympathetic nerve endings and of the cerebral cortex, and thus temporarily relieves fatigue and temporarily increases mental concentration and mental and physical efficiency. It has been used for the purpose of enhancing courage and endurance and for counteraction of mental depression, narcolepsy and the stuporous states induced by overdoses of alcohol, morphine and organic hypnotics. It is particularly to be recommended for the purpose of restoring to the normal the serious falls of blood pressure which occur in major operations from the use of anaesthetics, including spinal anaesthetics; the dosage used was from 0.01 to 0.02 gramme given intravenously or 0.015 to 0.03 gramme given intramuscularly (Ivy and Goetzl; Dodd and Prescott^{1,2}).

Toxicity of tannic acid

Recent experimental work has shown that intravenous injections of tannic acid and of sodium tannate into mice and guinea-pigs produce necrosis of the liver, and that the application of tannic acid to the raw area of burns in guinea-pigs causes slight liver damage (Barnes and Rossiter). Impairment of liver function after subcutaneous injections of tannic acid has been confirmed in rabbits by the galactose tolerance test (Clark and Rossiter). Its absorption from burns causes increased capillary permeability with haemoconcentration, loss of plasma protein and centrolobular liver necrosis (Cameron, Milton and Allen; Wells, Humphrey and Coll; Erb, Morgan and Farmer).

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ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also B.E.M.P., Vol. I, p. 1; and Cumulative Supplement, Key Nos. 1-11.

Diagnostic significance of pain**Differential diagnosis**

Conditions simulating abdominal emergency.—Gibson enumerates seven conditions prone to simulate abdominal emergencies, namely coronary thrombosis, diaphragmatic pleurisy, blood conditions, vascular lesions, renal conditions, sepsis elsewhere and tabetic crises. In coronary occlusion occasionally the pain is wholly abdominal, sometimes with vomiting and diarrhoea; collapse masks the cardiac signs. Coronary occlusion may mimic gall-stone colic and the electrocardiogram in gall-stone colic may mimic that of coronary occlusion. History, superficial tenderness and tenderness of the pectoral muscles may suggest cardiac origin. Embolism of the superior mesenteric artery from coronary occlusion is a true abdominal emergency. The coronary thrombosis, probably antecedent by several days, renders operation grave but it is essential. Diaphragmatic pleurisy accompanying the onset of basal pneumonia simulates abdominal emergency. The abdomen, rigid throughout, is more so above than below. The right iliac fossa is not more tender than the left but abdominal signs are unreliable. Appearance, herpes, pulse-respiration ratio, blueness, unilateral restriction of chest movement may indicate pleurisy. Radiography may help. When abdominal symptoms have appeared first in Henoch's purpura, operations have been performed. Rupture of the aorta and ruptured abdominal aneurysm are possibilities to remember. True abdominal angina from spasm in arteriosclerosis has so closely simulated abdominal emergency as to precipitate operation. An acute right-sided pyelonephritis and the pyelitis of pregnancy may resemble appendicitis. Tenderness over the twelfth rib is a valuable diagnostic point. Uraemic vomiting may suggest an acute abdominal condition and concomitant catarrh of the colon has simulated obstruction. Sepsis elsewhere, especially nasopharyngeal sepsis in children, and tubercular glands are associated with abdominal pain and sometimes rigidity. A radiograph may show enterospasm. Glands enlarged alongside the ureter causing colic may require excision. Tabetic crises are characterized by vomiting of food followed by clear liquid, with bile later and possibly blood, usually with epigastric pain. Examination of the pupils and reflexes preclude diagnosis of intestinal obstruction and gastric or duodenal perforation.

Diagnosis of acute abdominal emergencies**Value of early correct diagnosis**

Various methods of diagnosis.—Cope summarizes modern views on acute abdominal conditions. History, observation and palpation remain paramount for diagnosis. Stethoscope, sphygmomanometer and finger-stall are adjuvants. Peritoneal aspiration to identify infecting organisms is justifiable only in late cases receiving temporary conservative treatment. An inch incision under local anaesthesia remains preferable. Thereby an abdominal lesion can be differentiated from a thoracic lesion, imminent or actual perforation of the appendix detected and a suspected area digitally explored. The fluid obtained may suggest ruptured ectopic gestation, gastric, duodenal or appendicular perforation or acute pancreatitis. The blood sedimentation rate, normal with the appendix unperforated, on increase suggests pyelitis, mesenteric adenitis or other condition. A plain antero-posterior radiograph has sixfold possibilities, as follows. (1) Obstruction in the colon may be located by observing where the gut ceases to be gas filled; in volvulus the distension may be diagnostic; (2) in the small gut observation of fluid levels may clinch the diagnosis of mechanical obstruction; (3) a gall-stone occluding the small bowel may be recognizable; (4) gas accumulated sub-diaphragmatically from perforated stomach or duodenum may be seen, as may gas in abnormal positions from perforations of the small gut; (5) localization of the caecum may guide the incision in acute appendicitis; (6) in intussusception, a barium enema while screening the abdomen may confirm diagnosis, localize the lesion and effect partial reduction. Regional ileitis, apparently increasing, in the acute form is rarely diagnosed before laparotomy. Pneumatic injury produced by approximating the nozzle of a compressed air apparatus to the anus accidentally or in tragic fun is increasing. Diagnosis is easy but 50 per cent of patients succumb. Blast through air or water bruises or ruptures viscera. Lung involvement renders diagnosis difficult and prognosis poor. Analysis of 1,000 abdominal emergencies showed 763 approximately typical. Of atypical cases 150 were non-surgical simulations of abdominal disease and 76 atypical manifestations of common diseases; 11 represented rarities. Apyrexia, absence of vomiting and aberrant pain bring many elderly patients to the surgeon with an appendicular abscess developed. Prompt operation in children and for the unperforated appendix still obtains. Abdominal catastrophe, sometimes even haemorrhage, is less rushed than formerly; thirty minutes is well spent administering morphine and fluids to a shocked patient. Ochsner's method often precedes operation for peritonitis and the treatment of perforated peptic ulcer remains unchanged. Closure is rarely accompanied by simultaneous gastro-jejunostomy or partial gastrectomy. In acute obstruction of the small intestine aspiration of poisonous contents through the 'duodenal' rubber tube reduces toxicity and distention and with concurrent infusion reduces the perils of operation. Some obstructions even may be removed by this procedure but strangulation demands operation. The barium enema aids and, rarely, replaces operation in intussusception. Reduction under anaesthesia is watched through the

screen. An incision to ensure total reduction is advisable. In obstructed colon Paul's method of resection grows in popularity. Of the sulphonamides sulphapyridine is best for pneumococcal infections, for staphylococcal sulphathiazole and for streptococcal sulphanilamide.

Acute intestinal obstruction

Occurrence of blood in stools.—Anal fissure, associated with painful defaecation and readily detected by inspection, is the usual origin of bright red blood in the stools of infants and children. In order to illustrate less commonplace origins of blood in the faeces, visible or occult, Rosenblatt describes 6 cases. (1) An infant, aged 6 months, was suffering from an inflamed Meckel's diverticulum; during 36 hours before admission he evacuated two copious motions of material of the colour of prune juice. The resultant anaemia responded to blood transfusion, but within the next 36 hours 4 small dark stools were passed. This illustrates the alternation of major and minor losses. The admixture of blood with faeces and the fact that tarry consistency had not developed showed that the lesion was located in the ileum. An inflamed diverticulum successfully excised showed ulceration at its base. In case (2), which was one of strangulated hernia in an infant 8 weeks old, rectified by herniotomy, attention was drawn to the passage of blood and mucus but not of faeces or flatus. This feature obtained also in case (3) which was one of ileo-caecal intussusception. Severe pain, shock and often a palpable tumour may herald the passage of blood in this condition. The gangrenous bowel here necessitated a lateral ileocolostomy, which was subsequently closed. In case (4) Banti's syndrome, accompanied by massive tarry stools, was relieved by splenectomy. In case (5) a girl of 4 years suffered from bright blood in the stools with a tumour extruded after painful defaecation. Multiple polypi were scattered from transverse colon to rectum and colotomy was necessary for their complete removal. In case (6) chronic ulcerative colitis was responsible for visible and occult blood in the stools.

Peritoneoscopy

In diagnosis of liver diseases.—Benedict states that one of the chief uses of the peritoneoscope is in the diagnosis of liver disease. For the purpose of using the instrument only a 1-centimetre incision in the middle line above the umbilicus, made under local anaesthesia, is required. In 435 peritoneoscopies performed at the Massachusetts General Hospital there were 3 deaths, which were probably attributable to the procedure. In most of the cases the examination was made in order to ascertain the condition of the liver. In 260 cases of liver disease there were 170 metastatic carcinomas and 73 cirrhoses; the remainder of the cases showed various liver affections. The preparation for peritoneoscopy is important, for there is often jaundice and liver disease. Vitamin K is administered to reduce the bleeding tendency; it is safe to give chloral hydrate, but not morphine or barbiturates. The liver cases selected for peritoneoscopy include suspected metastatic carcinoma, primary carcinoma of the liver, hepatomegaly, ascites, jaundice, and those with doubtful clinical findings. In the author's 5 cases of hepatoma, the patients were all male; 4 had been taking alcohol regularly, 4 complained of epigastric or right upper quadrant pain; wasting and vomiting were present in 3 cases, jaundice and ascites in 2. With the aid of the peritoneoscope it is now possible to diagnose primary carcinoma of the liver or to make a differential diagnosis, which may be clinched by a biopsy.

Pneumoperitoneum

Value in radiological diagnosis.—Pneumoperitoneum may occur from pathological perforation of a hollow viscus after laparotomy, as an incident of tubal insufflation or as an accident in the induction of pneumothorax. Maxfield and McIlwain describe its surgical production and its value in radiological diagnosis. Cardiac insufficiency and acute infection alone forbid its employment and the reputed danger of gas embolism is very small when oxygen is used and it is nullified by using carbon dioxide. When examination is concentrated on bowel or kidney the simultaneous use of barium or diodrast is advantageous. The procedure, which is supplementary to other diagnostic methods, determines the shape and position of the abdominal viscera, defines peritoneal adhesions and implants and distinguishes ectopic from intra-uterine pregnancy and the retroperitoneal or thoracic from the abdominal tumour. Carbon dioxide, which is speedily absorbed, causes brief discomfort only but it requires to be used quickly. Air or oxygen do not add to the discomfort after paracentesis but in general they cause prolonged discomfort and should be confined to cases of massive ascites or those in which the difficulty of moving the patient renders rapid filming impossible. Deflation of the abdomen by reinsection of the needle after examination affords relief. The trocar through which the carbon dioxide is introduced after it has been bubbled through a solution of phenol, is inserted one inch below and one inch to the right of the umbilicus. The amount required rarely exceeds 2,000 cubic centimetres for the adult and 500 cubic centimetres for the infant. The apparatus is readily constructed. Radiographs are taken of the patients in the supine, the prone and in the right and left lateral decubitus positions. The injection of gas into the ruptured urinary bladder has differentiated intraperitoneal from extraperitoneal rupture. In pneumoperitoneum after laparotomy radiology may assist in distinguishing the resultant pain from that of pulmonary infarction and may decide cases of doubtful peptic perforation. Artificial pneumotherapy may be used in radiation therapy in order to remove the intestines from the field of radiation and in the determination of the X-ray portals so that the maximum intensity of the beam may be directed on the tumour.

General

Survey films in various conditions.—The use of survey films in the diagnosis of acute intra-

abdominal surgical conditions is reviewed by Levine and Solis-Cohen. At least 3 films should be taken, namely high, low supine and upright films. Views from the prone and lateral decubitus positions are also useful. In cases of a perforated viscus free air below the right side of the diaphragm is pathognomonic. Free air may not be seen immediately after perforation but it gradually accumulates. Survey films are often valuable in the differential diagnosis of coronary thrombosis or of ruptured abdominal aneurysm. In hepatocolic interposition haustral shadows may be seen and the appearances should not be mistaken for free air. In intestinal obstruction the more proximal the site of obstruction the greater is the degree of dilatation; a fluid level in the upright film is a valuable sign. When gas is present in both the large and the small intestines either there is a partial obstruction or the obstruction has become released; morphine medication, however, may lead to similar appearances. Other conditions in which survey films may yield valuable information include subhepatic abscess, perinephric abscess, pelvic abscess, lacerations of the spleen or liver, mesenteric thrombosis, volvulus, intussusception, and congenital intestinal lesions of the new-born.

Benedict, E. B. (1944) *New Engl. J. Med.*, **230**, 125.

Cope, V. Z. (1943) *Practitioner*, **151**, 65.

Gibson, A. G. (1943) *Practitioner*, **151**, 77.

Levine, S., and Solis-Cohen, L. (1944) *Surg. Gynec. Obstet.*, **78**, 76.

Maxfield, J. R., Jun., and McIlwain, A. J. (1944) *Radiology*, **42**, 346.

Rosenblatt, M. S. (1944) *Northw. Med.*, Seattle, **43**, 78.

ACANTHOSIS NIGRICANS

See also B.E.M.P., Vol. I, p. 75; and Cumulative Supplement, Key No. 14.

Clinical picture

Juvenile form

Report of two cases.—The infrequency of acanthosis nigricans prompts Peterkin and Jones to record 2 cases. Case (1) concerns a lance-corporal aged 24 years claiming to have been a fit man free from skin affections until he became over-heated during a cycle ride. He perspired freely and that night itching of the waist and armpits prevented sleep. He noticed a faint rash around the waist after a few days and during the next fortnight a darkening of the skin accompanied by thickening and corrugation in the armpits and groins and around the neck. On his admission to hospital histological examination confirmed the diagnosis of acanthosis nigricans. Medical examination including skiagraphy of chest and abdomen did not reveal any abnormality and his general health appeared to be unaffected but the gradual deterioration of the skin condition led to his discharge from the army. Case (2) was that of a private of the Auxiliary Territorial Service aged 20 who on admission to hospital with impetigo contagiosa was found also to have acanthosis nigricans. She displayed exaggeration of the natural skin lines, and crops of warty growths with pigmentation were present in the axillae and in the vulval region. Histology confirmed the diagnosis. Both cases appear to be of the benign or juvenile form of the disease without evidence of malignant growth or tuberculosis.

Adult form

Absence of vitamin C from blood stream.—Acanthosis nigricans is a rare disease of the skin and mucous membranes which occurs in two clinical forms, namely (1) the benign juvenile type and (2) the adult type which is generally seen in cachectic subjects with malignant visceral disease, with severe diabetes mellitus or with tuberculosis. Hollander reports a case which occurred in a woman aged 38 years and states that in the adult type of the disease severe avitaminosis may be a factor, especially as the characteristic skin lesions have been noted in connexion with other recognized deficiency states. In the case described vitamin C appeared to be completely absent from the blood stream. The woman was a Slav and suffered from an extensive eruption of the skin all over the body. When first seen she complained of irritation and of epigastric pain of about 15 months' duration for which she had been treated and had not obtained any relief. Increased pigmentation was present in the skin of the axillae, abdominal wall, neck and trunk. Later warty growths appeared and the patient lost weight and became weaker. A gastric carcinoma was discovered to be present. The entire skin was rough and dry; some areas showed hyperpigmentation and others depigmentation. Brownish-black and greyish-black warty plaques covered the backs of the hands, the nails were atrophic and the axillae showed darkly pigmented rugae. The neck was warty, and greyish excrescences were present on the edges of the eyelids. The lips were hidden by thick warty vegetations, which were also seen on the labia minora. Microscopically there was increased pigmentation of the Malpighian layer, with acanthosis and hyperkeratosis. After the patient had been given daily injections of vitamin B complex the warts on the eyelids and lips decreased in size. The patient died about 8 weeks after she was first examined. At a post-mortem examination the presence of an extensive adenocarcinoma of the stomach was confirmed.

Benign and malignant types

Association with carcinoma.—Although acanthosis nigricans is divided into both malignant and benign types Curth insists on their histological identity. Of 395 cases recorded, 50 per cent occurred in patients with malignant disease in another part of the body. These constitute the malignant type; the benign type comprised the 50 per cent who had not any associated disease. Acanthosis nigricans, which is never itself malignant, displays dark pigmentation of

the skin, with rugosity, papillomas and verrucose formations. The mucous membranes are sometimes involved. Predilection is shown by the disease for the axillae and the cutaneous folds generally. The histological features are hyperkeratosis, papillary hypertrophy and increased pigmentation of the basal layer. Its occurrence is world-wide and of equal sex distribution. The malignant type, which shows most often in the middle-aged, is symmetrical and spreading. The benign type is seen usually in the early years, is sometimes unilateral and after initial spreading is stationary or retrogressive. Sharp demarcation of type is impossible to find. As evidence that the co-existence of acanthosis nigricans and cancer is not fortuitous there is, first, the fact that simultaneous occurrence of the two is often met with. Secondly, the two diseases are generally of synchronous onset. Thirdly, regression in size or pruritus of the skin condition sometimes accompanies operative removal of the cancer. Finally, although cancer is generally a disease of advancing life, a group of 22 individuals the average age of which was 24 years is tabulated as suffering simultaneously from both diseases. One case here detailed, the ninth reported association of carcinoma mammae with acanthosis nigricans, emphasizes the extreme malignancy of cancer in this combination. In the other cases the accompanying cancers were gastric 50, uterine 8, hepatic 12, pneumonic 4, intestinal 4 and 14 various abdominal cancers. Scirrhus cancer in breast and stomach is 4 times reported. In 6 cases the growth was sarcomatous. Pressure of metastases on the sympathetic system, and disturbances of the adrenal and other endocrine glands do not throw any light on the causation of acanthosis nigricans. It appears that in malignant cases the cancer stimulates the cutaneous lesion and that the benign type is stimulated by one of the sex hormones.

Curth, Helen O. (1943) *Arch. Surg., Chicago*, **47**, 517.

Hollander, L. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 650.

Peterkin, G. A. G., and Jones, E. C. (1943) *Brit. J. Derm.*, **55**, 185.

ACCESSORY SINUSES OF THE NOSE

See also B.E.M.P., Vol. I, p. 77; and Cumulative Supplement, Key Nos. 15–17.

Malignant tumours of the maxillo-ethmoidal region

Treatment

Combined surgery and radiotherapy most effective.—Windeyer gives an account of the characteristics and treatment of malignant tumours of the upper jaw, that is carcinomas and sarcomas arising from the walls of or within the maxillary antrum, and ethmoidal tumours. A series of 153 cases is analysed; the incidence appears to be slightly higher in males. The aetiology is obscure but in some cases there was a history of chronic sinus infection. The clinical picture varies according to the stage of neoplastic involvement and according to the direction of expansion of the growth. In the author's series of cases which were histologically confirmed the ratio of carcinoma to sarcoma was 115 : 12. Metastases were found in the regional lymphatic glands and in distant organs in 38.6 per cent of patients; in 32.7 per cent there were cervical glandular metastases showing that glandular involvement is of fairly common occurrence in malignant conditions of the upper jaw, a fact debated by other observers. The diagnosis of such tumours is often not made until late in the course of the disease when severe destruction of the antral walls has already occurred. Rhinoscopy should be used in conjunction with ordinary methods of diagnosis and transillumination may also be useful. Diagnostic radiology may be a valuable means of confirming the suspected diagnosis and of demonstrating the extent of the lesion or the changes produced by treatment; it does not disclose early signs of recurrence. Biopsy must be carried out for confirmation of early lesions and it is also an aid in prognosis. In order to minimize the risk of metastasis the tissue should be excised by diathermy and the area should be coagulated. Preliminary irradiation may obscure the histological features and is better omitted. Radiotherapy, surgery and combined procedures have been used in the author's treatment, the last named having been found generally to be the most effective. The insertion of radium by interstitial implantation in some cases has given good results but has often caused necrosis. External irradiation by telerradium or by high voltage X-rays has been widely used and has usually caused very considerable regression or complete disappearance of the growth.

Windeyer, B. W. (1943) *Brit. J. Radiol.*, **16**, 362.

— (1944) *ibid.*, **17**, 18.

ACNE

See also B.E.M.P., Vol. I, p. 156; and Cumulative Supplement, Key No. 23.

Acne vulgaris

Treatment

Importance of hormone balance.—Ingram discusses acne vulgaris, essentially a reaction of puberty, which affects the face, ears, chest and back. Enlargement and hypersecretion of the sebaceous glands is accompanied by proliferation of the horny layer which obstructs the funnels of the pilo-sebaceous follicles. The trapped and inspissated sebum harbours staphylococci, diphtheroids and the acne bacillus and comedones or blackheads are formed. Secondary pyogenic infection leads to pustules and abscesses, with scarring and sometimes keloid formation. The pubertal factor concerns imbalance of the androgenic and oestrogenic hormones together with emotional embarrassments, of which acne is both the cause and the effect. Excessive carbohydrate intake, deficiency of vitamin B complex and constipation

require correction. Cocoa, chocolate, cheese, pig products and fried fats must be forbidden. Infections of the nose, throat and mouth demand attention. Differential diagnosis will consider oil acne, especially prevalent in war-time; inquiry eliminates bromide rash. Papulo-necrotic tuberculides which resemble acne affect the extremities as well as the face. Varioliform, necrotic or frontal acne occurs irrespectively of age and acne rosacea is seen chiefly during the menopause. In treatment thorough washing with a simple soap and warm water is adequate for skin and scalp. Short hair is preferable, but if not practicable in young women a weekly shampoo may replace daily head washing. The wearing of cotton garments next the skin is to be recommended. Steaming, medicated shampoos, ultra-violet therapy and vaccines are inappropriate but X-ray treatment is a useful adjuvant. Calamine lotions are effective. A suitable paste contains salicylic acid, sulphur, resorcin, zinc oxide and soft paraffin: greasy preparations generally should be avoided. Sulphathiazole is employed for secondary infections. Saturation with oestrogen although still tentative seems to offer good prospects of success in treatment. The presence of acne should be noted in deciding whether or not an individual is suitable for employment in the Tropics.

Ingram, J. T. (1944) *Practitioner*, **152**, 304.

ACTINOMYCOSIS

See also B.E.M.P., Vol. I, p. 173; and Cumulative Supplement, Key No. 26.

Treatment

Sulphonamide therapy

In pulmonary actinomycosis.—A case of pulmonary actinomycosis is reported by Pillsbury and Wassersug, in which sulphonamide therapy was of value. The patient, a woman aged 29 years, had had arrested pulmonary tuberculosis. Seven weeks after admission there were abscesses and sinuses on the left anterior chest wall. She was gravely ill. The erythrocyte count was 3,500,000; haemoglobin was 66 per cent; leucocytes were 22,000 with 86 per cent neutrophils, 7 per cent lymphocytes, 4 per cent monocytes and 3 per cent eosinophils. Sulphur granules were found in the sputum. She was given sulphanilamide 6 grammes and the next day 4 grammes and then for 19 days 3 grammes daily. For one month the condition appeared to be stationary. Then the giving of sulphanilamide, 4 grammes daily, was resumed for 16 days. Potassium iodide, which was given during both courses, was continued until the patient left hospital. Other sulphonamides were also given. Eleven months after admission the sinuses had all healed and the patient was discharged from hospital. She was examined 10 months after discharge; she was well and had gained 14 pounds in weight. She was still taking 5.3 grammes of potassium iodide daily. The authors state that as pulmonary actinomycosis is rare the diagnosis may be missed. This case showed that sulphonamide therapy brought about an improvement and enhanced recovery. It appears that the sulphonamides are more effective than are iodides in the treatment of actinomycosis.

Pillsbury, N. R., and Wassersug, J. D. (1944) *New Engl. J. Med.*, **230**, 72.

ACTINOTHERAPY

See also B.E.M.P., Vol. I, p. 180; and Cumulative Supplement, Key No. 27.

Technique

General irradiation

Therapeutic effects of various wave lengths.—Rollefson points out that the range of wave lengths in ultra-violet light usually available for causing photochemical reactions is from 4,000 to 2,000 Ångstrom units. Light in order to be effective in causing a reaction to occur must be absorbed. In dealing with complex systems the problem is often that of finding a wave length which will produce a desired effect without producing an undesirable action on some other substance present in the system. The author deals with four different effects of ultra-violet light from this point of view. The lethal action on micro-organisms was found to exert its maximum effect on *staphylococcus* and on *Chlorella vulgaris* at a wave length of about 2,600 Ångstrom units. Since the effective wave lengths are present in relatively small amounts in sunlight this source cannot have great germicidal powers; on the other hand the radiation obtained from mercury arcs is quite effective. In the formation of vitamin D from ergosterol maximum absorption of light is achieved at a wave length of 2,800. Although there is small absorption by ergosterol at the wave lengths present in sunlight the abundance of this light makes it an important source of the transformation. Two processes which accompany the formation of vitamin D are undesirable in the human system. These are the erythemic reaction (the third of Rollefson's considerations) and the transformation of vitamin D into toxic substances. The erythemic response shows its maximum at 2,960. The magnesium spark produces far less erythema than does sunlight or the mercury arc and offers a better source for therapeutic purposes, but the correct dosage will have to be determined by experiment. Finally Rollefson deals with hypericism in animals and while this is a harmful process it is possible that other sensitizers exist which will produce beneficial effects. The sensitizer is hypericin, a red fluorescent pigment contained in St. John's wort, and the effects of radiation occur at a range of from 5,400 to 6,100 Ångstrom units and so are outside the ultra-violet scale.

Rollefson, G. K. (1943) *Arch. phys. Ther.*, **24**, 664.

ADRENAL GLAND DISEASES

See also B.E.M.P., Vol. I, p. 232; and Cumulative Supplement, Key No. 30.

Adrenal hypoplasia and insufficiency***Incomplete syndromes***

Asthenia in women and the chloride excretion test.—Paschkis and Price have investigated the adrenal cortical function in 50 women with symptoms of asthenia, by means of the chloride excretion test originated by Cutler, Power and Wilder. It was thought that asthenia might in some cases be due to mild hypo-adrenalism, and that the adrenal dysfunction might be recognized by increased urinary chloride excretion after a diet low in sodium and high in potassium had been taken. Twenty-three out of the 50 patients did not actually complain of asthenia, and none of the patients suffered from any organic disease; the majority were psychoneurotic. A control study was carried out on 5 healthy women laboratory assistants. In the asthenic cases there was considerable variability in the urinary chloride levels whereas in the normal subjects little variation was seen. In the asthenic patients the variability could not be related to any change in symptoms or to menstrual function. In these cases there was also a great variation in the fasting blood sugar levels but there was no evidence of post-hyperglycaemic hypoglycaemia, which occurs in Addison's disease. Twenty-one of the patients had a low blood pressure. It was concluded that in asthenia there may be transient signs of a hypofunction of the adrenal cortex, which cannot however be regarded as symptomatic of a mild type of Addison's disease, and which is not the cause of the symptoms of exhaustion. The variation in the chloride excretion probably represents a somatic instability corresponding to the unstable personality of such patients.

Experiments in urinary excretion.—Stein and Wertheimer investigated the disturbances of water balance in the rat as the result of removal of the adrenal medulla. Water diuresis tests, water intoxication experiments and normal drinking tests were used. Urine excretion after a single water administration was abnormally slow and prolonged in medullectomized rats which evince none of the recognized symptoms of cortical deficiency. After the first post-operative month the inhibition of diuresis was less noticeable and excretion values equal to the normal minimum levels were recorded. Adrenaline abolished the inhibition of diuresis. In the water diuresis tests the amount of chlorine excreted was much increased as a result of the administration of adrenaline over that excreted by normal animals. Desoxycorticosterone acetate abolished the inhibition of diuresis only in very large doses and did not affect the chlorine excretion. Medullectomized animals were found to be far more susceptible to water intoxication than were normal animals. Adrenaline diminished and even abolished the difference in response between the two groups. Polydipsia and polyuria were pronounced in medullectomized rats in the second and third post-operative months and to a lesser extent subsequently; such disturbances were encountered in summer and spring but not in winter. The authors, in a discussion of the genesis of the pathological reactions, state that it is not yet possible to decide whether the insufficiency symptoms in the water balance are due to medulla deficiency or whether the action of adrenaline is secondary and merely equalizes the shock suffered by medullectomized and normal rats.

Hyperfunction of the adrenal cortex: hyperplasia and neoplasm***Primary carcinoma of adrenal cortex***

Estimation of hormone secretion as aid to diagnosis.—Anderson, Hain and Patterson record a case of primary carcinoma of the adrenal cortex with some peculiar features in a married woman, who gained nearly 2 stones in weight during the first year of her marriage; she died suddenly at the age of 25 from massive pulmonary embolism 2 days before the date fixed for operation. The place of the left adrenal gland was taken by a very large oval tumour (1,780 grammes) of rapid growth and of necrotic character but there were only mild symptoms of adrenal disease. The weight of the right adrenal gland was only half that of a normally functioning adrenal (3.5 grammes). The patient had a palpable tumour below the left costal margin and was treated hormonally for secondary amenorrhoea which had suggested pregnancy. At the necropsy one of the lobes of the liver contained a white metastatic tumour. The pituitary gland and the ovaries were normal; there were not any recent corpora lutea. The description of this case shows that a tumour of the adrenal cortex may be present without any hypersecretion of sex hormones.

Anderson, A. F., Hain, A. M., and Patterson, J. (1943) *J. Path. Bact.*, **55**, 341.

Paschkis, K. E., and Price, Alison H. (1944) *J. clin. Invest.*, **23**, 29.

Stein, L., and Wertheimer, E. (1944) *J. Endocrinol.*, **3**, 356.

AGRANULOCYTOSIS

See also B.E.M.P., Vol. I, p. 261; and Cumulative Supplement, Key No. 32.

Aetiology***Sulphonamide compounds***

Effects of sulphadiazine.—Since the introduction of sulphonamide therapy many cases of agranulocytosis have been reported as occurring after the use of sulphonamide compounds Sulphanilamide and sulphapyridine have most often been responsible, whereas very few cases have been recorded as occurring after administration of sulphathiazole or sulphadiazine. Nixon, Eckert and Holmes report 3 cases of severe agranulocytosis due to sulphadiazine; the patients were subsequently cured by continued administration of large doses of the same drug. Many observers have stressed the necessity of discontinuing the drug directly the bloo

count shows evidence of leucopenia. Others, who have noted transitory leucopenia in patients receiving sulphonamides have found that the leucocyte count became normal while the patient continued to be treated by the same compound. In fatal cases death is probably caused by gross infection associated with the absence of neutrophil corpuscles. For patients in whom recovery from agranulocytosis does not occur spontaneously various treatments have proved to be unsatisfactory. Blood transfusions, liver preparations and pentose nucleotide seem to be without beneficial effects. As the reduction in the leucocyte count in patients with severe bacteraemia who are receiving sulphonamides may be only transient, the use of sulphadiazine or sulphathiazole to overcome the infection appears to be justified if the depression of the bone marrow is of short duration. In the authors' cases 2 of the patients had scarlet fever and the third had primary atypical virus pneumonia. Although it was considered that sulphadiazine, which had been given in moderate doses for 2 weeks or longer, caused the agranulocytosis in each case, administration of the same compound was continued in larger doses to prevent a fatal termination from an overwhelming infective process. All 3 patients recovered. The authors recommend the continued use of sulphonamides, preferably sulphadiazine, in cases of agranulocytosis occurring during sulphonamide therapy until the normal protective functions of the bone marrow are again in action.

Nixon, N., Eckert, J. F., and Holmes, K. B. (1943) *Amer. J. med. Sci.*, **206**, 713.

ALCOHOLISM

See also B.E.M.P., Vol. I, p. 280; Interim Supplement, No. 15*; and Cumulative Supplement, Key No. 36.

The toxic effects of alcohol

Acute or subacute alcoholic poisoning

Chemical tests of blood and urine.—The reliability of chemical tests for alcoholic intoxication has been investigated by Ellerbrook and VanGaasbeek. Since June 1938 the local Police Department of an American town has arranged for routine tests of blood and urine in all persons charged with driving while under the influence of alcohol who are willing to submit to these procedures. In a series of 101 cases specimens of urine were obtained from 79 persons and of blood from 98. The results were of considerable confirmatory value, enabling the examining doctor to give his opinion with confidence and furnishing positive objective evidence for use in court. The authors' main conclusions may be summarized as follows. (1) The ratio between the alcohol concentration of the urine and that of the blood varies widely in individual cases. In a series of 76 persons examined it averaged 1.26 : 1, ranging between 0.69 and 1.71. It is thus impossible to calculate the alcohol concentration of the blood from that of the urine. (2) The tendency to accidents appears undoubtedly to increase with the blood concentration, which is probably closely correlated with the alcohol content of the brain. The authors have determined the alcohol concentration of the brain and of the blood in the right ventricle in 20 fatal accident cases, in most of which necropsy was carried out within 3 hours after death. The average ratio between the alcohol content (grammes per 100 cubic centimetres) of the blood and the alcohol content (grammes per 100 grammes) of the brain was 1 : 1. The range of values was from 0.88 to 1.52, representing various stages of absorption. The maximum value was obtained in a person who died after taking 5 pints of liquor for a bet. It is apparent, therefore, that the concentration of alcohol in venous blood is a good indicator of the concentration in the brain. (3) Capillary blood tends to give readings above those of venous blood and its use may possibly lead to an unjust accusation. (4) A fairly close correlation is found between the degree of intoxication as estimated clinically and the alcohol content of the venous blood. In the last 31 cases an attempt was made to guess the concentration of alcohol on the basis of the clinical signs. The difference between the guessed figure and that actually determined was never more than 30 per cent; in 71 per cent of the cases it was less than 15 per cent.

Ellerbrook, L. D., and VanGaasbeek, C. B. (1943) *J. Amer. med. Ass.*, **122**, 996.

ALLERGY

See also B.E.M.P., Vol. I, p. 302; and Cumulative Supplement, Key Nos. 40–52.

General diagnosis of allergic cases and identification tests

Aetiology and pathology

The psychological factor.—The psychological factor in asthma and allergic states is the theme of Brown and Goitein. Of two schools of thought the first regards the psychic factor as the cause of these conditions whereas the second regards psychological manifestations as effects, with the corollary that psychotherapy will here be unavailing. A group of 40 asthmatic patients and one of 40 patients otherwise allergic and a control group of 20 healthy persons were studied by clinical observation, by psychological biotyping, by the objective test battery and by psychiatric interviews. Assessment of their personality and their degree of mental integration was the aim. In the asthmatic group 57 per cent, in the allergic group 58 per cent and in the control group 90 per cent were classified as psychologically normal. In biotype, temperament, mood and secondary function the asthmatic and the allergic ran parallel. If overcome by nervous breakdown the asthmatic tended to obsessional neurosis and the allergic to anxiety states. The allergic were non-sinistral but the asthmatic showed a big percentage of

sinistrality and ambidexterity. The asthmatic group showed notably a constrained character, the percentage of 42 contrasting with a percentage of 15 in the control group. A conative secondary function attained 45 per cent in both asthmatic and allergic groups contrasted with 15 per cent in the control. In the asthmatic group magnanimity, poise, ambition for ascendancy and suppressed hate showed high percentages. The allergic group showed a character which was reflex and responsive and vivacity accompanied repression of ardour. These variations from the control group support, as regards asthma, the authors' earlier description of a 'respiratory personality' of distinctive pattern.

Eosinophilic infiltration as a cause of diverse syndrome.—Burckhardt and Kartagener report a case of a 37-year-old man who presented the syndrome of subacute epididymitis, pneumonic infiltration, prostatitis and eosinophilia hitherto described in only two instances. The patient gave a history of asthma dating from the age of 6 years. The attacks ceased at the age of 18 but recurred at the age of 36 after an acute sinusitis. At the same time he noticed a slimy discharge from the urethra after defaecation. A few days before he came under observation he had noticed a painful swelling of the left testicle. On examination he had no urethral discharge; the two-glass test showed both specimens clear and smears were negative for gonococci. The left epididymis was enlarged and tender, the prostate slightly enlarged and tender. The epididymitis improved during the next 4 days under treatment with cibazol (sulphathiazole). A urethral discharge appeared on the ninth day; no gonococci were found before or after provocative injection of silver nitrate. On the fourteenth day cough and dyspnoea developed and the patient was admitted to hospital with clinical and radiographic signs of patchy infiltration of both lungs. Three exacerbations of the pulmonary condition occurred before it finally cleared up. Blood examination disclosed an eosinophilia of 32 per cent. Numerous eosinophil cells were found in secretion expressed from the prostate and in the sputum. Ascarides ova were found in the stools and one worm was passed after treatment. The authors conclude that transient eosinophilic infiltration of allergic origin was the cause of the various manifestations.

Diagnosis

Skin tests: diagnostic value.—In his presidential address to the Society for the Study of Asthma and Allied Conditions, Tuft examined the diagnostic value of the various skin tests. Both the scratch and the intracutaneous methods have their merits and defects. Negative reactions to foods are comparatively more frequent after the scratch test than after intracutaneous injection, hence the latter method is preferable with these allergens but intracutaneous testing with certain potent allergens can be dangerous, especially in untrained hands. Skin tests in general are not an infallible guide; like other aids to diagnosis they must be considered in relation to the history and the clinical findings. A positive reaction implies past, present or future sensitivity to the allergen concerned so that in the absence of a proper history a patient's troubles may be pronounced to be due to some allergen with which he has not been in contact. Not all positive reactions are clinically significant. Evidence has been obtained that prolonged exposure to contact with allergens such as kapok or ragweed may induce cutaneous sensitivity in normal or allergenic subjects without necessarily causing clinical sensitiveness. The skin acts as a first line of defence and its tendency to become sensitized increases with advancing age. Moreover some allergens in sufficient concentration may cause non-specific positive reactions even in the non-sensitive subject. Extracts must therefore be so prepared and used in such dilutions that they do not produce positive reactions in non-allergic controls. All positive reactions should be checked at least once with either the same or a higher concentration to make sure of their specificity. Unless a positive reaction can be obtained repeatedly it cannot be considered specific. Negative reactions do not always prove that the patient is non-sensitive to the allergen in question and trial or elimination diets are a valuable aid.

Treatment

A gelatin vehicle for slow absorption of adrenaline.—Experiments have shown the advantages of slow absorption of adrenaline in conditions of shock and in the treatment of allergic states. Abramson describes a new and simplified method for the preparation of a gelatin vehicle in liquid form for subcutaneous injection of adrenaline, whereby a slow-acting pharmacological effect is obtained. The necessity of autoclaving the gelatin, a procedure required in other techniques, is avoided, and the gelatin is kept sterile and is liquid at room temperatures so that heating prior to injection is unnecessary; furthermore only half the usual quantity of gelatin is required. The method consists in adding sufficient urea to the gelatin solution to maintain the gel in the sol state at normal room temperature. Experiments on plasticity showed that an 8.5 per cent solution of gelatin together with 15 per cent of urea became liquid and remained so at room temperature after refrigeration. The mixture does not readily support the growth of bacterial organisms. It is possible that the adrenaline forms complexes with the gelatin and that the slow action of the drug may be due to slow breakdown of these complexes rather than to the retarding effect of the plastic mass of gelatin.

Allergic diseases

Respiratory system

Hay fever.—Spain, Fuchs and Strauss have prepared a gelatin-pollen extract which remains fluid at room temperature and is slowly absorbed. The viscosity of a gelatin solution decreases with prolonged heating in the autoclave. The authors used a gelatin mixture autoclaved at

20 pounds' pressure for 1½ hours, finding that this preparation could be injected through a No. 26 hypodermic needle. It has been used successfully for 90 patients. Mild reactions occurred in only 4. Gelatin-pollen extracts are particularly useful for treating patients who are so sensitive that they react badly to aqueous extracts.

Arthritis

Palindromic rheumatism.—The 34 cases of an unusual type of arthritis, palindromic rheumatism, which were described by Hench and Rosenberg in 1941 are now more fully reported on. The outstanding features are multiple apyrexial attacks of acute arthritis and peri-arthritis and sometimes also of para-arthritis with pain, swelling, redness and disability, generally of only one but sometimes of more than one small or large joint in an adult of either sex. Attacks appear suddenly and develop rapidly. They generally last for only a few hours or days and then disappear completely, but they recur repeatedly at irregular intervals. Despite frequent recurrences and the presence at times of an acute or subacute inflammatory polymorphonuclear exudate in the articular tissues and cavity, little or no constitutional reaction is shown by laboratory tests. There is not any significant functional, pathological, or radiographic change even after years of disease and scores of attacks. The incidence of the disease at the Mayo Clinic is 1 in 800 cases of rheumatism of all types, and the sexes are affected equally. The average age of onset of the disease is 35 years; before being admitted patients had been affected for from 4 months to 25 years (with an average of 7 years). Most patients have scores of attacks and some have hundreds, with an average of over 20 attacks a year. The rate of attacks varied greatly from patient to patient, and in any one patient. The duration of the attack was usually from a few hours to 3 days, but some of the very short attacks were painful. Attacks lasting for longer than a week were exceptional. The great majority of attacks were monarticular. Almost any joint in the body was liable to attack. At some time all patients had involvement of finger joints, mostly proximal interphalangeal joints. The dorsum of the hand was often affected. Knees were affected at some time in 32 cases, feet in 25, wrists in 23, shoulders in 22, ankles in 17, and elbows in 16. The spine is not involved. In most cases pain is severe, and there is articular redness. Disability in an attack is generally considerable, but there is not any fever or anorexia. The sites of the para-articular lesions are over the malleoli, bottoms of the heels, finger pads or distal phalanges, and proximal to the wrist (flexor surface). These lesions are regarded as distinct from those of angioneurotic oedema or urticaria. Intracutaneous or subcutaneous nodules were present in 3 cases. There was a tendency towards relative lymphocytosis between attacks. The blood uric acid was normal. The erythrocyte sedimentation rate was increased in about half the number of cases during attacks. The Wassermann reaction was negative. There were no significant changes in the joints on radiography. Biopsy observations showed that during an acute attack there was periarticular oedema and gross thickening of the capsule of the joint. Numerous polymorphonuclear leucocytes appeared in large numbers within the synovial membrane. As the attack subsided the exudate was absorbed. Then a brief period followed in which fibroblasts proliferated actively in the capsule and synovial membrane. Eventually the joint structures returned to the normal. The authors differentiate their cases from rheumatoid arthritis, fibrositis, intermittent hydrarthrosis, rheumatic fever, gout, angioneural arthrosis of Solis-Cohen and the allergic rheumatism of Kahlmeter. Numerous forms of treatment were tried and all proved to be relatively unsuccessful. As regards prognosis, 15 per cent of patients became free from attacks, 44 per cent improved, 26 per cent are unchanged and the rest are worse.

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AMENORRHOEA

See also B.E.M.P., Vol. I, p. 359; and Cumulative Supplement, Key No. 55

Aetiology

Secondary amenorrhoea

Due to endocrine lesions.—The prevalence of amenorrhoea in Central Europe during the 1914-18 war was then attributed to under-nourishment and overwork, with psychic influence as a minor contributor only. In studies of the condition made recently in a Philippine Internment Camp, Whitacre and Barrera found that endocrine disturbance was responsible, as the cessation of menstruation was too abrupt for food deficiency to have had that effect. Of 1,042 British and American women of menstrual age, 125 complained of recently developed amenorrhoea. Other catamenial disturbances were fewer. Of 60 nurses interned later, 14 reported amenorrhoea and 16 reported varied catamenial disturbance. Two subjects with a previously normal menstrual history, one being a virgin and the second a married woman with one child, were selected for laboratory investigation. The bulk of their urine was tested for the presence of oestrogen according to Marrian's method (acidification and benzene extraction), after the subtraction of the first morning specimen for gonadotropin investigation by Zondek's centrifugal supernation method. The test rats reacted to a dose of known oestrogen and to the urine of the first subject after menstruation returned. The test was there-

fore reliable when it showed a complete absence of oestrogen throughout the 15 days. In the gonadotropin determination it was found that the follicle-stimulating element was present, but the luteinizing element was not detected. Treatment of the amenorrhoea patients was handicapped by lack of supplies, but recovery was spontaneous in the majority. The supply of oestrogenic substance was reserved for patients displaying symptoms of the menopause. A small supply of vitamin E was administered to 10 patients in the form of wheat-germ oil for 10 days preceding the expected menstrual flow; a menstrual period, or uterine haemorrhage, resulted in 8 cases and pain premonitory of menstruation but without consummation in one case. These effects were probably due to suggestion. The value of psychotherapeutic treatment, in a condition caused by psychic shock, worry and fear acting through the autonomic nervous system, is recognized. Administration of oestrogenic substance to replace the element shown to be absent is a more rational treatment than that of gonadotropin shown to be present.

Treatment

General

Prostigmin as a specific.—Friedmann investigates the claims of American workers that prostigmin is specific in producing a menstrual flow in cases of delayed menses which are not due to endocrine dysfunctions, systemic conditions or pregnancy. The rationale is that hyperaemia, the result of oestrogenic action on the uterus, coincides with the liberation of acetylcholine by the hormone and thus produces the vasodilatation. The parasympathetic nervous system controls the hyperaemia and can readily be upset by physical, mental and emotional causes, giving rise to a non-endocrine form of amenorrhoea. The diminished production of acetylcholine can be rectified by the administration of prostigmin. Friedmann selected his cases in accordance with the requisites mentioned above. He found that the age of the patient and the length of the menstrual delay had not much influence on the results and that the character of the previous menstrual cycle, which should have been quite regular or have shown only a slight variation, was of greater importance. Prostigmin was reliable in its action in 94.5 per cent of 36 cases. In 30 cases of pregnancy prostigmin was without effect. Controls were treated by the injection of sterile water in lieu of prostigmin and menstruation did not ensue in any. The technique consisted of one intramuscular injection of prostigmin, 1 milligramme, on 3 successive days, the treatment being discontinued if after the first or second injection the menstrual cycle was restored. The periods were normal in quantity and duration. A number of patients experienced unpleasant secondary effects of the injections but they were of mild degree.

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AMPUTATION

See also B.E.M.P., Vol. I, p. 378.

General aims and ideals

Satisfactory healing

Notes on the guillotine amputation.—Kirk and McKeever consider that the guillotine amputation is based on 'the sound surgical principle of drainage for infection'. The procedure saved many lives in the war of 1914–18. Closed amputations of extremities which are traumatized beyond repair are dangerous to life, even when sulphonamides are employed locally and systemically. The guillotine method is the operation of choice when severe joint infection, infected compound fracture or extreme trauma interfering with the circulation of the tissues, necessitate amputation. There are two stages. The first consists of the removal of the damaged portion of the extremity and the second is that of making the final stump suitable for prosthesis. (1) A slightly concave open cross section of the extremity, with the skin slightly longer than the underlying muscle, is carried out. At the point of retraction of the deep layers of muscle the bone is cut through, and a cuff of periosteum is not removed. The entire cross section is left open. Skin traction is absolutely essential in post-operative treatment and must be kept up continuously so that the skin is gradually pulled down over the muscles. (2) When there is an area of clean granulation tissue covering the bone end and bacteriological studies are satisfactory, preparation of the stump for use of a prosthesis is conducted. The scar is excised *en bloc* to good skin and the skin is undermined in order to mobilize it and is sutured over the end of the bone. A thin section of bone may require to be removed if the scar is so firmly attached to it that to cut it loose would leave a projecting piece of bone under the closed skin. Occasionally a plastic section of skin has to be done after it has been mobilized thoroughly in order to cover the end of the stump. Sulphonamides are given as a matter of routine in secondary closures, if such are subsequently indicated.

Satisfactory function of stump

Essentials of a good stump.—According to Perkins, the limb-fitting surgeon coordinates the physiological knowledge of the operating surgeon with the engineering skill of the limb-maker. Unless he can guarantee a stump which will fulfil the requirements of the limb-fitting surgeon, the surgeon should perform two amputations, (1) provisional and (2) final. Provisional amputation should be done as low as possible, preserving unsoiled the tissues that will be cut through at the final amputation; infection matters little provided it traverses vital tissue, since drainage ensures healing. Unsutured skin-flaps afford speedier and less painful

healing of the stump than do guillotine operations. Final amputation should be delayed until clinical observation rather than bacteriological culture gives a guarantee of primary healing. The limb-fitting surgeon's ideal below the knee stump measures $5\frac{1}{2}$ inches from knee joint level to the end of the tibia; a 2-inch stump is the functional minimum. The ideal above the knee stump should measure 11 inches from the great trochanter. A stump of less than 9 inches lacks adductor power. A short stump necessitates the wearing of a tilting-table limb; disarticulation at the hip leads to difficulties. The forearm stump should measure 7 inches from the olecranon process and the humeral stump 8 inches from the acromion process. Disarticulation at the shoulder and wrist amputations are unfavourable mechanically. The ideal stump is attained by (1) semicircular, equal, antero-posterior skin-flaps, (2) reflection of skin and deep fascia in one layer, (3) transverse section of the muscles half an inch below the site of bone section, (4) sawing the bone flush with the retracted muscles, (5) careful haemostasis, (6) suture of the two layers of deep fascia and (7) closure of the skin. An adherent scar, infolding skin, redundant soft tissue, a protruding spur of bone and a tender stump are thus avoided. Training of the patient in the use of the prosthetic limb is the final necessity.

General technique

Choice of anaesthetics

Refrigeration and chilling.—O'Neil describes a method of amputation of limbs without anaesthesia other than that produced by refrigeration of the part to be amputated. He surrounds the extremity distal to a tightly applied tourniquet with crushed ice encased in rubber sheeting and by this means maintains its skin temperature at $8-10^{\circ}$ C. for several hours. The limb can then be amputated painlessly and there is almost complete freedom from shock. The adoption of this technique in a series of 50 cases in which, owing to the presence of marked peripheral arterial insufficiency, advanced age or rapidly spreading gangrene or sepsis, spinal or general anaesthesia would have been hazardous, was found by the author to lead to a distinct reduction in the mortality rate. Furthermore, this chilling process, by lowering metabolism, not only enabled a tourniquet to be applied for as long as 12 hours, but also greatly improved the patients' mental and physical condition; amputation was often deliberately delayed in order to allow time for such improvement to occur. There were indications too that refrigeration would allow of successful amputation at levels much lower than is usual. A circular amputation from 10 to 15 centimetres below the level of the tourniquet was the operation of choice. Drainage was never employed, as a guillotine amputation without closure was considered preferable. After operation the temperature of the stump was returned to the normal slowly by the gradual removal of ice bags. Local chilling of the tissues without the application of a tourniquet also proved to be of value in inhibiting sepsis and in averting gangrene and retarding thrombosis when occlusion of peripheral arterial trunks was in progress. It never prevented the necessity of amputation however once the part had become devitalized. It is suggested that this form of therapy, by reason of the inhibition of bacterial growth and prevention of pain, shock and oedema, may have possibilities as an adjunct in the treatment of burns and of various other injuries.

Hinchey states that refrigeration therapy has been advocated for arteriosclerotic gangrene with circulatory insufficiency, uncontrollable limb sepsis and severe trauma to the limbs with damaged circulation. He describes its use in three surgical cases. (1) In a case of sepsis of the arm, gangrene of the hand had set in. There was no radial pulse and the patient was cyanosed and extremely toxic. A light tourniquet was applied to the upper arm 7 centimetres below the shoulder and the arm was packed in ice. After 20 hours, temperature, pulse and respirations were nearer to the normal and the patient was generally improved. Amputation was performed, after morphine premedication, without anaesthesia. A further $\frac{1}{4}$ grain of morphine was given during the amputation. Although the patient was awake throughout, he did not complain. Recovery was complete. The use of refrigeration and of the tourniquet prevented septic absorption and gave the patient time to recover from shock before the amputation, thus probably saving his life. (2) In a case of severe crushing compound fracture of 3 fingers with much tissue damage, in a child aged 9 years, the hand was packed in ice after debridement and dusting with sulphanilamide. Refrigeration was maintained with gradually lengthened intervals for 12 days. There was not any sepsis but circulation was not restored, so the fingers were amputated. (3) The third case was that of a 70-year-old man with mild diabetes mellitus and arteriosclerotic gangrene of both legs. One leg was amputated under cyclopropane and nitrous oxide anaesthesia. A month later the second leg was amputated under ice anaesthesia with the usual sedation. The patient felt the cutting of the sciatic nerve but otherwise there was no pain. There was no post-operative shock and the pain was about the same as after his first operation, but nausea and vomiting were a little more pronounced. Wound healing was uneventful. The author states that the tourniquet is essential to obtain adequate anaesthesia by ice refrigeration. Its use, which amounts to physiological amputation, prevents toxic absorption from a septic limb. The tourniquet also helps to lessen the shock resulting from a damaged septic limb. Indications for the use of ice refrigeration are arteriosclerotic gangrene, sepsis, war wounds and cases of limb trauma with arterial spasm. Here the icing helps the limb to survive. In cases of immersion foot, therapeutic icing to a lesser degree cools the hyperaemic painful feet during the early stages; such cooling is also useful for frost-bite. Refrigeration anaesthesia has been used by another investigator when skin grafts were being taken from the thigh.

Artificial limbs

For lower limb amputations

Description of modern appliances.—Thomas points out that modern skill has brought no more useful aid to humanity than prosthesis, particularly of a limb. It is the responsibility of the surgeon to advise the patient on his permanent prosthesis and to supervise the fitting of the appliance. Many surgeons fail to accept this responsibility. The surgeon should be familiar with the standard types of joint control mechanism. The problem of emotional adjustment is made easier by the continued interest of the surgeon and his cooperation with the limb maker. The advantages of temporary prosthesis in hastening the shrinkage and toughening of the stump are emphasized. Improperly placed operative scars, deficient or excess bone length, redundant muscle, tight skin flaps and exposed nerve ends all tend to make fitting difficult and the result unsatisfactory. The artificial leg usually consists of four components: (1) socket, (2) knee piece, (3) skin piece and (4) foot. Into the socket the stump is carefully fitted. The wood socket is covered with rawhide; metal sockets are not in common use. Knee motion is controlled by a 'muscle' strap of leather with elastic at either end, which is attached to the pelvic belt and passes over a roller fastened to the shin piece inside the knee. Side joints at the knee are used in amputations below the knee. The foot is usually made of wood with a joint in the forefoot of rubber belting and with limited motion at the ankle. Rubber pads are placed in heel, instep and forefoot. It is difficult to produce a comfortable prosthesis for patients with amputations in the region of the knee or ankle. The Syme amputation also presents difficulties. The socket for a stump through the knee joint is usually made of heavy leather, with a front opening for lacing and with a felt pad on the end for weight bearing. The author stresses the importance of the proper fit of the stump and the correct alignment and length of the limb as the guiding considerations.

Prostheses for children

Need for early fitting.—In an article on prostheses for children Craft emphasizes the great advantage from every aspect—psychological, physical and economic—of fitting a child amputee with an artificial limb at the earliest possible age: in the case of a leg from the age of 3 years, of an arm from the age of 5 years. It is a mistake to delay the fitting until the child has ceased to grow. The main object of the article is to bring to the notice of all authorities who have any responsibility for such children the scheme sponsored by the Board of Education and the Ministry of Health, and approved by the Government, to provide each child who requires it with a correct type of artificial limb. Under the scheme children may be admitted to Ministry of Pensions Hospitals for expert surgical treatment, and may be provided with the best possible artificial limb through Queen Mary's Hospital, Roehampton, in conjunction with the various government and child welfare authorities. As it is necessary for limbs to be renewed as the child grows, parents are helped by the scheme to bear the necessary expense. Craft bases his remarks on some years' intensive study and practical work at Roehampton. In the case of an amputation, the site of operation must be chosen carefully and subsequent growth taken into account. The stump should be suitable for the fitting of a normal prosthesis, instead of a temporary unadjustable appliance. Child patients quickly become expert in its use if they are fitted soon after operation and can get about and behave like normal children. Because of their activity it is especially important in the case of children to avoid scar tissue at any position of pressure, friction and weight bearing. On about the third day after operation slow movements of the stump should be begun, and the duration and range of movement should be increased daily. Correct bandaging of the stump, after removal of the stitches, is necessary.

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ANAEMIA

See also B.E.M.P., Vol. I, p. 408; and Cumulative Supplement, Key No. 59.

Pernicious anaemia

Atypical

Difficulties of diagnosis.—Schwartz and Legere¹ describe atypical pernicious anaemia affecting 9 young women of whom 5 were negroes. All exhibited the characteristic blood and bone marrow changes, gastric achylia and response to liver treatment but exceptional features caused hesitation in diagnosis. Acute rheumatic fever, subacute glomerulo-nephritis, subacute infective endocarditis and aplastic, haemolytic, aleukaemic and splenic anaemia were alternatives considered in different cases. The abnormalities emphasized comprise (1) age incidence, (2) unusual proportion of negroes, (3) acute onset, (4) prominence of cardiac symptoms, (5) pyrexia suggesting infection and (6) absence of neurological features. Age ranged from 17 to 35 years whereas pernicious anaemia usually affects those beyond the third decade. The proportion of negroes exceeds remarkably the 8 per cent ratio hitherto admitted to the same hospital. The acute onset of the disease in 4 cases contrasts with Cabot's finding of only 28 acute onsets in 1,200 cases. Cardiac symptoms led to a diagnosis of rheumatic fever in

8 cases. In 5 of these a subacute infective endocarditis was postulated, negatived later by sterile blood cultures. In 7 cases pyrexia exceeded 102° F. whereas Cabot found pyrexia prominent in only 3 of 1,200 patients although it was noted as present in 475 of 691. Ankle and patellar clonus was shown in one patient only. Haematological changes conformed to type with the exception of the colour indices which ranged from 1·3 to 0·6 although a low index is admittedly rare. Rare too is a coated tongue, noted once. The spleens of eight patients were palpable whereas Cabot notes only a 20 per cent incidence of splenomegaly. The benefits of transfusion in pernicious anaemia are transient only.

Treatment

Importance of Castle's factor.—Schwartz and Legere² suggest that previous attempts to evaluate massive dose therapy and the storage of the liver principle in cases of pernicious anaemia are inaccurate, because they fail to take sufficient account of the inexplicable and often prolonged remissions which are so characteristic of this disorder, even when it remains untreated. Fifty-four patients who had a recurrence of symptoms after a previously diagnosed relapse had been successfully treated with liver therapy were therefore observed. It was found that in every case secondary relapse had been brought about by a discontinuance of treatment, that the interval between the cessation of treatment and the onset of a subsequent relapse varied from 2 to 38 months and that this interval was remarkably inconstant even in individual patients. The investigation failed to demonstrate any relation between the length of this interval and the duration of previous treatment, the average dose or total amount of liver administered during treatment or the age, sex or race of the patient. The authors suggest however that the length of time which elapses before any individual relapse occurs is probably connected intimately with the quantitative secretion of Castle's intrinsic factor, the quantity of extrinsic and other essential dietary factors and the storage of the anti-pernicious principle in the liver. Some other factor as yet unknown must also operate, since investigation failed to demonstrate any correlation between the relapse time and the average amount of liver extract necessary for maintenance.

Hypochromic deficiency anaemias

Idiopathic hypochromic anaemia

Clinical report of cases in young males.—Thomson describes hypochromic anaemia affecting 9 lads of between 17 and 19 years of age and one man of 45 years. Causation was lacking and there was not a family history of anaemia. All had received adequate diet before and during the war and not one gave a history of haemorrhage. All had pursued normal activities and occupations, accepting pallor as their natural complexion. Although generally small and immature not one complained of symptoms except slight dyspnoea in the most serious cases. A haemic systolic apical murmur was usually heard. The spleen was just palpable in 4 patients and noticeably enlarged in one. Blood examination, taking an average of the 7 patients kept under supervision, showed before treatment a haemoglobin index of 52 per cent on Haldane's scale and a mean erythrocyte diameter of 6·9 microns. The erythrocyte count averaged 4·4 millions per cubic millimetre. The corresponding figures after treatment were haemoglobin 108 per cent, mean diameter of erythrocytes 7·4 microns and erythrocyte count 6·13 millions per cubic millimetre. Although one patient escaped deficiency of gastric acidity 5 displayed complete achlorhydria and 4 significant hypochlorhydria, suggesting relation between the gastric deficiency and anaemia. Response to iron, administered usually in the form of 2 fersolate tablets thrice daily, was highly satisfactory. The duration of treatment ranged from 5 weeks to 12 months. Sufficient time has not elapsed to determine the desirability of a maintenance dose.

Aplastic anaemia

Pathology

A condition of erythroblastoma?—Limarzi and Levinson report on a hitherto undescribed type of erythropoiesis observed in the sternal marrow of a man who was admitted to hospital with normocytic anaemia and suppurative prostatitis and who died after a suprapubic cystostomy. The marrow showed 2 distinct types of erythrogenesis: (1) normoblastic, with normal bipolar mitosis as the mechanism of cell division; (2) pathological, characterized by multiple mitosis, multinucleated erythroid cells and cells with bizarre nuclear forms. The pathological type appeared to originate in giant erythroblastic cells which also are capable of producing normal erythroid cells. These giantoblasts are so abnormal in appearance as to suggest that they represent a cancerous development of the reticulum differentiating on haemoglobiniferous lines, that is erythroma or erythroblastoma. None of the abnormal cells appeared in the blood. The rapid conversion of the megaloblastic marrow in pernicious anaemia to normoblastic marrow after liver treatment is explained by production of normoblasts from multinucleated erythroblasts.

Haemolytic anaemias of the new-born

Aetiology

Erythroblastosis foetalis and the Rh factor.—Of 10 guinea-pigs immunized with rhesus monkey blood Hoare obtained satisfactory serums from 3 for the purpose of testing 1,122 unselected blood donors. The serums possessed titre active to dilution of 1 in 60, sufficient to eliminate confusion arising from anti-A or anti-B agglutinins. Two volumes of serum to

one of cell suspension were used. Results were determined by the sedimentary pattern after the liquid had been standing at room temperature for over half an hour and by microscopical examination of the resuspended sediment. In later work serum and cells after standing at room temperature for over half an hour were shaken and spun at from 500 to 1,000 revolutions per minute for a period up to 2 minutes. Examination of the deposit for agglutinates by tapping the tube confirmed previous tests. Of the donors 949 (84·6 per cent) proved to be Rh positive, AB 27, A 349, B 90, O 483 being the group distribution. Among 173 (15·4 per cent) Rh negative donors AB 3, A 64, B 14, O 92 was the group distribution. The percentages tally with those of Wiener and of Boorman, Dodd and Mollison. Notes appended on 5 cases of erythroblastosis foetalis report in each case an Rh positive father and infant, with an Rh negative mother displaying Rh antibodies. The erythrocyte count was always below 2·15 millions per cubic millimetre and a haemoglobin index of 50 per cent was the highest recorded. One infant was admitted too late for transfusion. After transfusion one recovered but 3 succumbed.

Pathogenesis

The new Hr factor.—Levine reviews the pathogenesis of erythroblastosis foetalis. The essential factors are (1) the response of the Rh negative mother to the foreign Rh positive foetal blood by production of anti-Rh agglutinins and (2) the continuous passage of maternal anti-Rh agglutinins through the placenta to react with and to haemolyse the susceptible foetal Rh positive blood. The Rh factor is a mosaic of several antigenic substances, known as Rh₁, Rh₂, and Rh' in the terminology of Wiener and Landsteiner. In most cases the father of an erythroblastotic infant is Rh₁, occasionally Rh₂. Levine also discusses an atypical agglutinin produced by an Rh positive mother of an erythroblastotic infant. This agglutinin reacted distinctly on all Rh negative and Rh₂ bloods. This new factor is called Hr and its corresponding antibody anti-Hr. If an Rh positive father is homozygous (RhRh), the foetus in every pregnancy must be Rh positive and each pregnancy offers an opportunity for the immunization of the Rh negative mother. If a father is heterozygous (Rhrh) there is an equal chance of the offspring being Rh positive or Rh negative. In either mating the first one or perhaps two pregnancies with Rh positive foetuses will be required to initiate a sufficient degree of iso-immunization. Once the Rh negative mother is immunized, all subsequent Rh positive foetuses will develop some clinical form of erythroblastosis. Thus there will be a low incidence of the disease in some families and a high one in others. All children may be normal if the mother is genetically incapable of producing antibodies. Affected infants are transfused with Rh negative blood, but not with the mother's blood. The rapidly increasing jaundice and anaemia in the neonatal period is puzzling. It has been suggested that the source of the anti-Rh agglutinins may be colostrum, but many such infants are not breast fed. There is justification for replacing the term, erythroblastosis foetalis, by the term, haemolytic disease of the foetus and the new-born.

Clinical picture

Critical reviews of the three main types.—Gilmour describes 52 cases of erythroblastosis foetalis, particularly from the aspect of morbid anatomy and with many references to the literature. He groups the cases into three types, (1), (2) and (3), which correspond to those recognized as hydrops foetalis, icterus gravis and congenital anaemia. The three types are shown to be varieties of a single disease by the fact that more than one type often occurs in siblings, and by certain common chemical and pathological features. The differences between the types may depend upon differences in the severity of the disease and in the age of its onset. (1) In this type the mothers were usually in middle life and had had several previous pregnancies; many of the infants had been still-born or had died early. Albuminuria, oedema and hydramnios are very often found in these mothers. Hydrops foetalis is found in foetuses or in infants who live for not more than 36 hours. A feature peculiar to this disease, which does not occur in the other two types, is lipid infiltration of the suprarenal cortex. (2) This type occurs in infants at birth or in the first weeks of life. They are rarely still-born and may recover. Jaundice is a constant pathological change and nuclear jaundice, areas of necrosis in the cerebral white matter and jaundice of the renal medullary pyramids are peculiar to this type. (3) In contrast to hydrops foetalis and icterus gravis, the incidence of miscarriages, still-births and early deaths without obvious erythroblastosis was not great in families into which infants with congenital anaemia were born. This type is found in infants who survive the first 3 days, and is shown by pallor and anaemia, which are present at birth or appear in the first 3 weeks. Jaundice is common but relatively mild and oedema is always absent at birth and usually is absent later. That the disease depends upon a hereditary factor is shown by its familial incidence. The effect is chiefly on the hepatic and haemopoietic tissues. Areas of necrosis occur in the liver; there is also increase of reticulin, or diffuse fibrosis, retention of bile in intracellular canaliculi or in liver cells, or possibly fatty degeneration. The effect on haemopoiesis is shown by anaemia, excessive numbers of erythroblasts in the blood, haemosiderosis of the liver and excess of haemopoietic tissue. Most cases of erythroblastosis depend upon the rhesus factor—an agglutinating present in the blood of 86 per cent of the population but in only 8 per cent of mothers of infants with erythroblastosis.

The rhesus factor.—A group of 19 infants with haemolytic disease and 2 with congenital hydrops were investigated by Langley and Stratton. Their clinical, pathological and serological findings agree with those of other workers that the presence of a foetus whose blood

is Rh positive in an Rh negative mother with the production of an anti-Rh agglutinin in the mother's blood is the causal factor of the syndrome of haemolytic disease of the new-born. In 19 of the 21 cases an anti-Rh agglutinin was found in the maternal blood. In 7 out of 10 samples of breast milk from the mothers the anti-Rh agglutinin factor was present. The authors confirm that there is not any relation between the titre of maternal agglutinins after childbirth and the severity of the disease in the infant. Many of the clinical signs of haemolytic disease in the new-born may be absent. Serological methods have detected cases which were clinically or pathologically very mild. The combination of Rh negative mother and Rh positive child occurs in 10 per cent of pregnancies, but erythroblastosis foetalis occurs in only one case in 438. Probably some additional factor is present to account for this such as the response to the immunizing effect of the foetal antigens after transplacental passages or the ability of the foetal antigens to cross the placental barrier. The authors recommend that only Rh negative blood should be used by maternity flying squads since in emergencies blood typing is impracticable. They suggest that panels of Rhesus negative donors should be prepared to meet this need; such a panel has been arranged for the North-West Regional Transfusion Service.

Rare type of Rh antibody.—Race and Taylor give the clinical details of a family in which haemolytic disease of the new-born was caused by a rare type of Rh antibody. This antibody has proved to be of fundamental importance in the recognition of allelomorphs of the Rh gene and the resulting genotypes. On rare occasions haemolytic disease of the new-born has been caused by the presence in an Rh positive mother of a sort of anti-Rh serum which agglutinates the red cells of all Rh negative and some Rh positive persons. This serum has been named anti-Hr (Rh reversed). Race and Taylor describe a patient with haemolytic disease, the mother of whom was Rh positive and had in her serum an antibody similar to, but not identical with, anti-Hr. This serum, which is called St by the authors, reacts with the blood of 80 per cent of people including all the Rh negatives, all the heterozygotes Rhrh and some of the homozygous Rh positives (RhRh). The reactions are now known to be due to the presence in the erythrocytes of factors determined by allelomorphs of the Rh gene. By using St and other forms of anti-Rh serums it has been proved possible to determine serologically the genotype of about 80 per cent of people. The blood group of the patient was O MN. P⁻, Rh⁺, St⁺; that of the mother was O MN. P⁻, Rh⁺, St⁻ and that of the father A, MN. P(?), Rh⁺, St⁺. The child recovered after 3 blood transfusions had been given, and it appeared that St negative blood which was given in the second and third transfusions survived longer than did the St positive blood which had been given in the first transfusion. The mother was given a transfusion of St negative group O blood and had no reaction.

Investigation of hepatic function.—Salmon and Richman aver that haemolysis as sole explanation of icterus gravis neonatorum, is inconsistent with the disparity of blood destruction and hyperbilirubinaemia and with the known ability of the normal liver to excrete more bilirubin than physiologically it ever has to excrete. Placental degeneration, renal relation to bilirubin excretion and capillary permeability also require consideration but attention is here concentrated on hepatic function, investigated by the bromsulphalein and cephalin-cholesterol tests. Of the unselected infants investigated almost all exhibited an icterus index above the normal. Arbitrarily they were classified into those above and those below an index of 20. Visible icterus depends not upon a high transitory index but upon the continuous elevation of the index. Packed cell volume determinations showed wide individual variations and did not show correlation between degrees of haemolysis and of icterus. In the bromsulphalein test 2 milligrams of dye per kilogram of body weight were injected in 1 per cent solution into a scalp vein. Blood drawn at intervals showed equally rapid excretion in the groups having indices above and below 20. Moreover comparison with other workers' results proved the infantile liver to be commensurate with the adult liver in this respect. To the cephalin-cholesterol flocculation test for parenchymatous hepatic disorder performed as outlined by Hanger, both groups gave positive readings during the first few days of life, becoming negative towards the end of the first week of life. Similar reactions in the mothers during the post-partum period indicate a common causation operating before delivery. Interpretation of these findings is not yet possible.

Treatment

The rhesus factor.—Nickerson and Moulton describe two new-born babies with erythroblastosis foetalis of the icterus gravis neonatorum type resulting from iso-immunization to the Rh factor, who recovered after transfusion with Rh negative blood of the proper blood group. The agglutinin operating in the Rh phenomenon has a very narrow range of temperature specificity; it operates at body temperature but not at ordinary room temperature. Cross matching should be done at 37.5° C. for at least 30 minutes. The mothers were not allowed to nurse the infants, on the assumption that the anti-Rh substance might be transmitted through the breast milk. The maximum icteric index in the patients was 600 and 700, but after 4 months there was not any evidence of damage to the central nervous system from kernicterus. When the deciduous teeth erupted they were a deep greenish colour in each child. The authors test as a routine measure in early pregnancy for Rh factor and for blood group. If the mother is Rh negative or if there is a history which suggests past iso-immunization in pregnancy, blood from the husband and from siblings is tested for Rh factor and for blood group. If the mother is Rh negative and the father Rh positive, the mother's serum is tested

bi-weekly from the seventh month for anti-Rh substance. Demonstration of a significant and rising titre warrants prompt delivery of the baby if viable, so as to prevent excessive flooding of the foetal blood stream with anti-Rh substance. The authors' impression is that infants who do not show any evidence of erythroblastosis but whose mothers have anti-Rh factor in their serum, do not do as well as was expected—perhaps because of the presence of the anti-Rh factor in the breast milk.

Race, Taylor, Cappell and McFarlane report on the Rh factor in erythroblastosis foetalis affecting 50 families. Of the population 85 per cent are Rh positive and 15 per cent Rh negative yet the mothers of erythroblastotic infants are 90 per cent Rh negative, many displaying an antibody to the Rh factor. This is convincing evidence that the Rh factor is implicated. An Rh positive male, if homozygous, begets Rh positive offspring only but if heterozygous he has offspring which have an equal chance of being Rh positive or Rh negative. If he, mating with an Rh negative woman, begets an Rh positive foetus iso-immunization in the mother may produce an antibody destructive to the foetal erythrocytes. This is not inevitable, for 1 pregnant woman in 10 is Rh negative and carrying an Rh positive foetus, yet the occurrence of erythroblastosis is very rare. In these 50 families 44 mothers were Rh negative and of them 38 displayed anti-Rh agglutinins. If the Rh factor was not concerned in causing erythroblastosis 7 or 8 in 50 would be the normal Rh negative proportion. One pregnant woman in 5 has an agglutinin for an antigen of the ABO system of groups in her foetus. Again the infrequency of erythroblastosis shows that in such case production of an antibody destructive to the foetal erythrocytes is not inevitable but the presence of 6 Rh positive mothers among these families is evidence of its possible happening. Four first-born children of these 6 Rh positive mothers were affected, due perhaps to the iso-agglutinins being already present in the mother. Of first-born children of Rh negative mothers one only was affected; 38 were unaffected; there were 5 still-births or miscarriages. Here 2 or 3 Rh positive children seem generally to precede an Rh negative child. The complete absence of Rh negative children among the 49 tested children of Rh negative mothers is emphasized.

Successful blood transfusion in erythroblastosis foetalis.—Newerla recounts the successful issue of blood transfusion in a case of erythroblastosis foetalis. When a woman having Rh negative blood, having mated with an Rh positive man, becomes pregnant of an Rh positive foetus, her blood occasionally produces antibodies haemolytic to the foetal erythrocytes; such haemolysis is the basis of erythroblastosis foetalis. In the patient, a male infant, the first two of the three characteristics of this syndrome developed—icterus, anaemia and hydrops—on his ninth day. To explain the occasionally delayed onset of haemolysis the ingestion of colostrum has been invoked. Here that explanation is untenable as the infant was bottle-fed. Storage of the antibodies in the foetal tissues and their later release by a mechanism unknown must be postulated. The father, who had had jaundice in infancy, belonged to blood group A, the mother and infant to group O; there was one previous child in good health. The mother's blood proved to be Rh negative and to contain anti-Rh agglutinins. The antibodies are neutralized within a fortnight if the infant survives but to promote survival repeated transfusion of erythrocytes is necessary. These should be Rh negative erythrocytes, such being indestructible to the maternal antibodies. In this case blood for the first two transfusions was supplied by a professional donor of group O, the Rh factor being disregarded. The improvement in the blood picture was not entirely sustained until the third transfusion. The blood for this containing cells compatible by Levine's modified cross matching technique, was given by the mother's sister. Immediate amelioration of the anaemia and final disappearance of the normoblasts ensued and on examination two months later cure was considered to be established.

Survival time of transfused erythrocytes.—Mollison points out that knowledge of the survival time of transfused erythrocytes in normal infants is a physiological essential. He studied the survival time in haemolytic disease of the new-born, using a technique based on the differential agglutination method of Ashby. In 8 out of 9 cases of icterus gravis neonatorum in which transfusions were given during the first 14 days of life Rh positive erythrocytes were eliminated from the infant's circulation within 10 days of the transfusion. In 4 cases in which Rh positive erythrocytes were transfused after the fourteenth day of life destruction was less rapid. Rh negative erythrocytes transfused to 21 infants with haemolytic disease survived for not less than some 80 days in all but one case. In most cases the elimination is uniform at the rate of about 1 per cent of erythrocytes per day and the total survival time is approximately 100 days. The same survival rate was found after transfusion in (1) a normal infant who had an acute haemorrhage shortly after birth when the ligature slipped off the umbilical cord, (2) a child aged 11 months with nutritional anaemia and (3) a child aged 15 months with aplastic anaemia. A similar survival rate is found in adults. Blood from adult donors was used for transfusions. When an infant with haemolytic disease of the new-born has to be given transfusions, Mollison recommends the use of Rh negative blood of its own group when serological tests have been made and it is reasonably certain that destruction is due to anti-Rh agglutinins. He advises group O, Rh negative blood when tests have not been made and group O blood when destruction is thought to be due to anti-A or anti-B agglutinins. When destruction is due to agglutinins other than atypical anti-Rh, group O blood compatible with the mother's serum is probably the safest to use. In every case direct matching of the donor erythrocytes against the mother's serum is desirable before transfusion is carried out.

Normocytic anaemia**Deficiency of production**

Aetiology of anaemia associated with infection.—Saifi and Vaughan conducted an investigation into the aetiology of anaemia associated with infection. The peripheral blood was studied in (1) mild, (2) acute and (3) chronic infections and plasma bilirubin estimations were made. (1) In mild infections (10 cases) neither anaemia nor reticulocytosis was present. (2) The anaemia of acute infections (20 cases) was never megalocytic or hyperchromic in type, the reticulocyte count was usually raised and the serum bilirubin was within normal limits. (3) Similarly, in chronic infections (14 cases) no instance of megalocytic hyperchromic anaemia was observed, the reticulocyte count was always raised and the average colour index was 0.7; the serum bilirubin was never raised. Iron or iron and liver therapy was without effect so long as the active infection persisted. Necropsy material was studied in 11 acute and 4 chronic cases. Marrow hyperplasia was the rule and in 4 acute cases iron was deposited in the spleen and the marrow and to a lesser extent in the liver. In chronic infections leucoblastic activity of the bone marrow, neutrophil myelocytes predominating, was constant. All cases also showed considerable erythroblastic activity. The authors discuss the theories of the causation of the anaemia. The evidence of active erythropoiesis seen at necropsy was a refutation of an aplasia of the bone marrow as the aetiological factor and observations of pigment metabolism did not show any convincing evidence of increased haemolysis. The writers are of the opinion that deficient erythrocyte production is the basis of the anaemia, since the absence of mature erythrocytes from islands of erythrocyte activity in the marrow was remarkable in their cases; the infection is thought to interfere with the synthesis of haemoglobin which results in a maturation defect of the marrow.

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ANAESTHESIA

See also B.E.M.P., Vol. I, p. 472; and Cumulative Supplement, Key No. 60.

Choice of anaesthetic**The nature of the operation**

Ether versus cyclopropane in abdominal surgery.—Eisenhart, Simpson and Gillespie have investigated the incidence of circulatory complications after operations performed under cyclopropane or ether. The cyclopropane group included 257 upper abdominal and 1,268 lower abdominal operations; for the ether group the corresponding figures were 435 and 531. Abdominal operations were chosen for study because they, and especially upper abdominal operations, require deeper anaesthesia than do others. It was found that with both ether and cyclopropane the incidence of circulatory complications was greater after upper abdominal than after lower abdominal operations. With ether the greater the incidence the deeper the anaesthesia. With cyclopropane this is true of lower abdominal operations and is probably true of upper abdominal operations unless 'controlled respiration' is used. After upper abdominal operations the tendency to circulatory complications is greater when cyclopropane is used. This applies to major and minor complications and to the fatal cases. It applies moreover to patients with normal circulatory systems and in greater degree to those known to have before operation some cardiovascular disease. In the case of lower abdominal operations the evidence suggests but is not statistically strong enough to prove that cyclopropane is more likely than ether to be followed by circulatory complications.

Inhalation anaesthesia

Statistics of 228,000 cases.—Gillespie discusses to what extent deaths on the operating-table are attributable to the effects of operation and to what extent to the effects of anaesthesia. In 2 of 7 case reports given, both anaesthesia and operation appeared to have been responsible. In 3 cases death was due to the operation. In 2 others the anaesthetic was the cause of death; in one, although there was not any respiratory obstruction, deep anaesthesia had diminished respiratory exchange and additional oxygen had not been given; in the other, as there had been difficulty in maintaining a free airway the endotracheal tube should probably have been left in place until the patient had recovered consciousness. The anaesthetist in this second case should not have handed the case to a student but should have made sure that anaesthesia was

light and that the patient's airway was properly safeguarded after operation. The author observed that fatalities decreased as the anaesthetist's experience increased. In his series of 13,000 anaesthetics, which were given over a period of 10 years, there were about 30 patients who were not expected to survive the operation. The majority did recover from the anaesthetic, although they died soon afterwards. The author analyses in all about 228,000 cases drawn from 5 different teaching hospitals on 3 different continents. The mean mortality during operation was just over 1 case in every 1,000. In one hospital with an almost equal mortality rate the anaesthetics had been given by experienced medical men. In another hospital in which the mortality rate was below the average a consultant staff usually had administered the anaesthetics. In summing up Gillespie states that when every type and sort of case is taken into account, death before recovery from the anaesthetic is about 1 in every 1,000 and that when the grave cases are treated by experienced anaesthetists the mortality is less than when they are undertaken by junior men.

Use of trichlorethylene in open circuit.—The use of trilene (trichlorethylene) in a closed-circuit machine for inhalation anaesthesia appears to fall into line with the carbon dioxide absorption technique. Carden says that trilene is dangerous when it is used in this way but that there is not any apparent risk when it is used in an open circuit. From evidence in cases of palsy after administration of trilene anaesthesia by closed circuit, he concludes that toxic oxidation products are formed by the interaction of soda-lime and trilene. The reaction was speeded up by increased warmth. Trilene used without the soda-lime canister, that is in an open circuit, showed no oxidation products. Analysis showed no deleterious substances in cyclopropane or trilene but whereas the former gave no reaction when passed through soda-lime, trilene gave off a sour smell which was probably due to the formation of dichloroacetylene, a potentially toxic product. The caustic soda content of the soda-lime and its hygroscopic qualities vary with different brands, and this important difference was responsible for the occurrence of the trigeminal and other cranial nerve palsies which occurred with trilene anaesthesia administered by the closed-circuit method.

Review of methods in use

Elam says that accounts of disasters occurring under anaesthesia seldom appear in medical journals. He mentions several cases of deaths which occurred under intravenous anaesthesia and suggests that the newer anaesthetic techniques may be even more dangerous than chloroform is now supposed to be. The general opinion seems to be that spinal anaesthesia is of value but that its routine use in uncomplicated cases is to be deprecated. The use of barbiturates by intravenous administration has increased of recent years. Opinions differ about their safety in use but undoubtedly many deaths have occurred as a result of their administration. Pentothal sodium should be used only in hospital where everything is ready for an emergency. Local anaesthesia is not entirely free from risk. Although many dentists use nitrous oxide gas, Elam points out that in some machines the percentage of N_2O to O_2 shown on the flowmeters does not bear any relation to the percentage which the patient is actually inhaling. Cyclopropane although valuable has two drawbacks, (1) it is explosive and (2) the anaesthetist must have long experience before he can obtain adequate relaxation by its use. Ether is the oldest anaesthetic agent and still remains the safest. The author states that there is no prospect of agreement regarding the safety and the suitability of spinal anaesthesia. He suggests that deaths on the table and all untoward incidents which occur during operation should be discussed with entire frankness. The anaesthetist should be prepared for every emergency that may arise in the operating-theatre.

Ether anaesthesia

Methods of administration

A new ether adsorber described.—There is always the risk of an explosion if ether is used as the anaesthetic agent in the vicinity of electrical equipment or near an open fire. This risk is increased if a number of successive operations are performed under ether in a small and ineffectively ventilated room. Epstein points out that this danger can be greatly reduced by passing the exhalations of the patient through certain kinds of activated charcoal which adsorb the ether vapour. With the help of diagrams he describes in detail the construction of a medium and of a large capacity adsorber to contain this activated charcoal and shows how ether can be incorporated into the anaesthetic apparatus used when giving ether by the closed method. On the average the medium size can be used for 1 hour 10 minutes, the amount of ether administered to the patient being about 8 fluid ounces, before exhaustion of the charcoal occurs. The capacity of the large adsorber is a little more than twice that of the medium size. Clinically, exhaustion of the charcoal is indicated when ether can be detected by the nose in the outflow from the adsorber. The exhausted charcoal can be regenerated if an electric oven with a temperature regulator is available, otherwise it must be discarded. Adsorbers improvised from a Waters canister and from a Service respirator can be used for about 17 or 20 minutes before exhaustion of the charcoal occurs, during which time from 2 to 3 fluid ounces of ether will have been administered.

Spinal anaesthesia

Scope and limitations

Nupercaine in general surgical practice.—Brown discusses the use of spinal anaesthesia in general surgical practice. He employs this method in 50 per cent of his operations. The uncertainty regarding the level of anaesthesia obtained and its duration has disappeared

since the introduction of nupercaine. Untoward sequelae in the central nervous system have never been encountered by the author, who considers the possibility of their occurrence to be greatly exaggerated. In the author's cases the patient is given an injection of morphine grain $\frac{1}{4}$ and hyoscine grain $\frac{1}{100}$, 1½ hours before the operation; an hour later he receives an injection of morphine grain $\frac{1}{10}$ and hyoscine grain $\frac{1}{100}$. Should the operation area be below the umbilicus, 2 cubic centimetres of 1 in 200 nupercaine are given, whereas if above the umbilicus 12 cubic centimetres of 1 in 1,500 strength are administered while the patient is sitting. In the former case the patient is immediately laid flat, whereas in the latter he is held upright for 25 seconds. In all cases ephedrine grain $\frac{1}{4}$ is given intramuscularly. Brown is so much impressed with the importance of premedication that he prefers to use general anaesthesia in caesarean section, since the heavy doses of morphine necessary before spinal anaesthesia may be harmful to the baby. A great advantage of premedication is the almost complete dissociation of the patient from his environment and the lack of all unpleasant memory of the ordeal. Post-operative vomiting and depression of urinary output in prostatic conditions for a day or two are disadvantages. Brown considers that emotion plays an important part in the production of fall of blood pressure; the dissociation induced helps to avoid this and its influence is augmented by the institution of a technique of silence during the operation. He also regards emotional stress as an important cause of failure of the anaesthetic drugs to act. The problem of headache and backache after spinal anaesthesia has not yet been solved. In his cases headaches now occur less often and the author attributes this fact to the better type of needle employed, to the use of nupercaine and to the adoption of the recumbent position for a relatively prolonged period. Pulmonary embolism would appear to be a grave risk after spinal anaesthesia and prolonged post-operative immobility, but in 1,800 major operations under general, local and spinal anaesthesia Brown has seen only 5 fatal cases due to this cause.

Technique

Novocain (procaine hydrochloride).—Lee describes a method of continuous spinal analgesia which he has used in 105 cases. The advantage of the continuous method is that the dose can be adapted to the needs of the patient and of the surgeon and to unforeseen changes in the scope or the duration of the operation. In this series the drug used was a hyperbaric solution of 5 per cent procaine hydrochloride (novocain) in 5 per cent glucose, injected into the spinal theca in serial doses. Prior to operation pholetone (pholedrine) (10 milligrams, for the purpose of maintaining blood pressure) and a basal narcotic were administered. A special mattress, part of which is cut out under the lumbar spine, is required for the operating-table. The needle is introduced by means of a Rowbotham's introducer into the selected intervertebral space with the patient in the left lateral position. The needle is provided with a tap and remains in position throughout the operation. When cerebrospinal fluid drops from the needle the initial dose, usually from 100 to 150 milligrams, of procaine-glucose solution is given, the stylette is replaced in the needle and the patient is turned on to his back. When the anaesthetist has removed the stylette and satisfied himself that cerebrospinal fluid emerges from the needle the latter is connected by rubber tubing with the syringe containing the analgesic solution. The height of analgesia is controlled by the amount and rate of the injection, the level at which it is given and the tilt of the table. A rough estimate of dosage is 1 milligram of procaine hydrochloride for each pound of body weight. Injections are given about every half-hour as required. Light general anaesthesia can be used if desired. Blood pressure readings did not differ from those obtained when a one-dose technique was used. The incidence of post-operative headache was the same. No deaths referable to the anaesthetic method occurred in this series.

Continuous spinal anaesthesia.—Recent advances in the successful use of continuous spinal anaesthesia and present-day modifications in its administration are described by Hingson, Ferguson and Palmer. The authors have used this method of anaesthesia in 5,150 cases, that is in 30 per cent of all operative cases treated during a period of 5 years in the Marine Hospital, New York. In a comparative study of 10,000 surgical cases, the safety of spinal anaesthesia was found to be equal to that of general anaesthesia. The anaesthetic preparations used were spinocain (procaine in a special solvent), pontocaine hydrochloride (butethanol), metycaine (hydrochloride of γ -(2-methyl piperidino)-propyl benzoate), and nupercaine. The surgical cases in which spinal anaesthesia was used included orthopaedic operations on the lower limbs, hernioplasty, rectal and lower urological cases, intraperitoneal lower abdominal operations and upper abdominal lesions. In 144 of the cases supplementary general anaesthesia (generally pentothal sodium) was also used. Two deaths occurred in the entire series. High spinal anaesthesia was used in 42 instances; in such cases there is a danger of sudden transient hypertension, which may be succeeded by total vascular failure unless preventive measures are taken immediately. Various neurological sequelae were noticed, such as persistent cranial nerve palsy (one case), peripheral nerve palsy (3 cases: 2 temporary, one chronic) and hyperaesthesia and hyperalgesia (14 cases; the majority recovered spontaneously). Haemorrhagic meningitis occurred in one instance after 4 attempts at lumbar puncture had been made, but the patient recovered. Headache was complained of by 1 per cent of the patients. A considerable fall in blood pressure occurred in patients in whom the anaesthetic was allowed to ascend higher than the eighth thoracic segment; it was however successfully treated with vasopressor drugs. Nausea during operation under spinal anaesthesia may be

combated by giving vasopressor drugs and oxygen inhalations. The advantages of continuous spinal anaesthesia appear greatly to outweigh the disadvantages, if a careful selection of cases is made.

Continuous caudal anaesthesia.—Continuous caudal anaesthesia is recommended by Southworth and Hingson as a safe and controllable procedure in the hands of experienced anaesthetists. The technique is easily learned, but a knowledge of the variations of the sacral hiatus is required in order to reduce risks of failure. The effects on respiration and blood pressure are minimal in most cases although certain precautions should be observed. Caudal anaesthesia has not been used for children, and aged subjects require 20 per cent less of the drug than is needed for robust individuals. Metycaine (the hydrochloride of γ -(2-methyl piperidino)-propyl benzoate), procaine hydrochloride (novocain) and pontocaine hydrochloride (butethanol) have been used; procaine hydrochloride was found to cause slight nervous irritability in some cases. Possible toxic effects after rapid absorption include (1) central nervous irritation and convulsions, (2) circulatory collapse and (3) allergic manifestations. Three types of procedure are described, namely low caudal, mid-caudal and high caudal block. The first is used for perineal, transurethral, urological, gynaecological and lower spinal anaesthesia, and therapeutically for thrombophlebitis, vasospastic conditions, sciatica and low-back strain. Mid-caudal block is used in inguinal, ventral and femoral hernioplasty, pelvic operations, caesarean section, phlebectomy, fractures or amputations of the legs, appendicectomy, operations on the knee and hip joints and other miscellaneous procedures. High caudal block may be utilized for neutral hernioplasty, various upper abdominal operations, cholecystectomy and rib resection. In abdominal operations good muscular relaxation is obtained by caudal anaesthesia. The post-operative condition of the patient is very satisfactory; a few patients complain of slight transitory soreness in the back. The main disadvantage of the method is that it takes some time to carry out. Infection at the site of injection may be prevented by sealing the junction of the needle and the skin with sulphathiazole ointment. Supplementary inhalation anaesthesia or intravenous anaesthetics may be used if required. Continuous caudal anaesthesia was effective in 96.7 per cent of 903 cases supervised by the authors.

Local anaesthesia

Regional anaesthesia

Novocain (procaine hydrochloride) in painful states.—In an analysis of skeletal pain treated by novocain (procaine hydrochloride) injection Gorrell emphasizes that relief of pain does not abolish the responsibility for determining a possibly serious underlying cause. Rheumatic conditions, osteoarthritis and sprains provided 236 of the 295 cases treated. The essentials to success are identification of underlying conditions, auxiliary treatment in the form of exercises and injection of the cardinal points. The painful area is palpated to detect, and mark, such points as cause the patient to wince. Areas which require multiple injections foreshadow less success than does a case which displays one cardinal painful point. Novocain in 1 per cent solution was usually employed by Gorrell or a 1 in 1,000 solution of the longer acting nupercaine. Numbital grains $1\frac{1}{2}$ may be given before the injection; the patient should remain recumbent as injection of 10 cubic centimetres or more sometimes causes faintness. A wheal is raised by injecting 5 drops into the skin with a fine needle. A 24-gauge 2-inch or 3-inch needle is then substituted and inserted through the wheal until bone is reached or pain is experienced. Two cubic centimetres of novocain are injected and if after half a minute pressure no longer elicits pain that cardinal point has been treated sufficiently. If tenderness persists the needle is projected further and the process is repeated. To ensure that all cardinal points have been treated the motions which previously caused pain are gone through as a test. Injections may be repeated every 3 days. Two injections sufficed to relieve half the number of patients. Unless each injection produces a progressively longer relief the suitability of the method must be reconsidered. The patient should expect a probable temporary reaction within 6 hours, for which analgesics should be provided. The patient should be given advice concerning posture, weight reduction and cognate matters. Occasionally there is a focal sepsis which needs to be removed.

Rectal anaesthesia and basal narcotics

Basal narcotics

Technique of intravenous administration.—Three types of barbiturate are employed for the purpose of inducing anaesthesia, prolonged, sustained or short. As an example of each Bray cites sodium amytal, nembital and pentothal sodium. Intravenous anaesthesia may serve as the sole anaesthetic, precede inhalational anaesthesia or supplement spinal anaesthesia. The single dose or repeated dose or the continuous method of administration is employed. Barbiturate anaesthesia is ideal in operations on the head and neck and is unsuited only to children, dyspnoeic subjects and cases in which profound relaxation is required. Veins suitable for injection in the arm remote from the surgeon should be selected. Generally $1\frac{1}{2}$ grains of seconal, or in alcoholic subjects nembital, are given overnight and repeated in the morning, supplemented before operation by an injection of morphine and atropine. Pentothal sodium, the barbiturate to be preferred, is dissolved to form watery solutions of from 2.5 to 5 per cent and when effervescence subsides the syringes are loaded. The upper arm is encircled with the armlet of a baumanometer which remains in place throughout the operation. Through a

wide-bore needle 2 cubic centimetres of solution are injected in the period of 30 seconds; the reaction determines the subsequent rate of injection. Swift unconsciousness usually prevails. Coughing and retching are rare and must not be allowed to hasten the giving of the injection. A metal airway is introduced and oxygen is administered through a nasal catheter. The repeated dose of the anaesthetic, with the needle kept in the vein and an occasional withdrawal of blood into the syringe to ensure its potency, is to be preferred to the single dose. The continuous method is reserved for debilitated patients and cases in which difficulty is expected. Through a cannula tied into the exposed vein glucose-saline is administered by drip. The barbiturate is injected by syringe into the tubing above the cannula. In emergency, coramine can be administered or blood transfusion made through the cannula. Vomiting occurred occasionally during recovery in the author's cases, but complications, immediate and remote, were negligible. One death due to respiratory obstruction occurred in 700 administrations.

Intravenous pentothal sodium with continuous oxygen inhalation.—French analyses 837 administrations of pentothal sodium-oxygen anaesthesia lasting from 20 to 180 minutes. Emergency operations or those on patients with shock are not included. Pentothal sodium, or sodium ethyl thiobarbiturate, forms a clear yellowish solution in distilled water. This should be freshly prepared and any cloudy solution discarded. Pharmacologically the drug depresses the central nervous system and respiratory centre, causes vasodilatation and, with rapid intake, blood pressure falls. Hepatic and renal diseases do not forbid its use. Morphine and atropine precede administration. A tourniquet is adjusted to the arm and a 20-gauge needle, attached to a 20 cubic centimetre syringe, is inserted intravenously. During the first 15 seconds 2 cubic centimetres of a 5 per cent solution are injected while the patient counts. If no idiosyncrasy manifests itself meanwhile, slow injection continues until the patient ceases counting. A B.L.B. mask with respiratory bag is applied while the anaesthetist supports the jaw; 4 or more litres of oxygen are inhaled each minute. If respiration is satisfactory more solution is injected. Induction occupies from 3 to 5 minutes. Dosage varies with the patient's physical condition. From 1 to 2 grammes maintains an hour's anaesthesia. Obtundation of the laryngeal reflexes may require a mechanical airway. Overdosage causes respiratory failure necessitating clearance of the airway, artificial respiration and respiratory stimulants. Post-operative attention and support of the jaw must be unremitting until the reflexes return. No fatalities occurred in this series. The time of recovery varied with the amount administered. Post-operative vomiting occurred in 30 per cent of patients. Post-operative complications do not exceed those of other anaesthetics. Slight local reaction affected the site of injection in 6 patients. The muscular relaxation and quiet breathing resulting from the use of pentothal sodium promote operative speed. This anaesthesia is also appropriate to old age, debility and pulmonary disorders. The desirability of having 2 anaesthetists, the necessity of post-operative attention and the exclusion of the very young constitute its disadvantages.

Intravenous pentothal sodium in ophthalmic practice.—From a review of the literature on the use of intravenous pentothal sodium anaesthesia in 54,831 cases, together with data obtained from its use in 106 ophthalmic operations, Post and Robertson conclude that this light or short-acting barbiturate supplies a safe and satisfactory form of anaesthesia which has no very definite contra-indications and which is compatible with all other anaesthetics. Its effect on the circulatory system is minimal although it does produce a certain respiratory depression which can be minimized appreciably by the administration of oxygen in all cases and by injecting the drug intermittently in order to allow time for detoxification. From the patient's point of view it provides an induction which varies from a few seconds to 2 minutes and is free from excitement and a recovery which is free from vomiting. The technical difficulties inherent in dealing with the smaller veins of children as well as their poor cooperation and the uncertainty of their reaction to barbiturates make this form of anaesthesia unsuitable for use in patients below 9 or 10 years of age. Statistical data are given of 106 ophthalmic operations in which the use of pentothal sodium anaesthesia proved to be satisfactory, a temporary apnoea which occurred in 2 instances and which quickly yielded to artificial respiration and an injection of coramine, being the only serious complication encountered. In all cases a pre-operative opiate was given and a 2.5 per cent solution of pentothal sodium was used both for induction and for subsequent doses. Most of the patients received in addition the local anaesthesia ordinarily employed. The fact that 14 of the 17 patients who did vomit after operation had received an opiate pre-operatively raises doubts about the advisability of such pre-operative treatment especially in intra-ocular surgery in which vomiting is extremely hazardous.

General

The Oxford anaesthetic vaporizer

Value in maxillofacial operations for war wounds.—Rushton, describing his Tunisian experiences of endotracheal anaesthesia with the Oxford vaporizer in a maxillofacial unit, classifies 120 cases in 2 groups each of 60 cases. Pentothal was used for induction in group (1) and omitted in group (2). In both, 70 minutes was the average duration of operation, and there was not any instance of chest complication or of death. In group (1) the average consumption of anaesthetic was pentothal 0.25 gramme, chloroform 0.25 fluid ounce and ether 4 fluid ounces. Slight post-operative vomiting ensued in 5 per cent of patients. In group (2)

an additional ounce of ether was consumed. Slight vomiting occurred in 12 per cent of patients. Six hours' starvation, if practicable, was followed by injection of morphine with atropine or hyoscine. Hyoscine engendered a quiet and pleasant induction. Induction with ether in the vaporizer was slow and subjectively unpleasant. From trial of various methods there emerged as most satisfactory the intravenous injection of 0.25 gramme of pentothal followed by chloroform and ether mixture on the open mask. After intubation the patient is connected with the vaporizer and anaesthesia is deepened, to pack the throat, by setting the ether concentration to 15 per cent for a few minutes. Thereafter a setting of between 5 and 10 per cent maintains the anaesthesia required. The vaporizer receives a small flow of oxygen in prolonged operations. Repetition of anaesthesia, often demanded in maxillofacial surgery, requires an anaesthetic such as can be faced with equanimity. A known constancy of ether vapour, elimination of rebreathing and portability are an advantage to the anaesthetist.

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ANEURYSM

See also B.E.M.P., Vol. I, p. 501.

Aneurysm of the aorta (thoracic and abdominal)

Aetiology

Aneurysm in youth and in pregnancy.—A dissecting aortic aneurysm which developed on the twelfth day after parturition in a woman aged 22 years led Schnitker and Bayer to examine the literature with special reference to the occurrence of the aneurysm in youth and in pregnancy. Of 580 recorded cases 141 patients were under 40 years of age; of these 49 were females, 24 of them pregnant. In causation, hypertension was more salient in the elder group. In the younger group hypertension was absent in half the number of cases of which records were available, including the authors' own patient. Traumatic causation also has perhaps been over-emphasized. In the authors' patient a mild blow sustained 3 years previously seemed to be of negligible importance and at the time of seizure she was seated, but in 12 of the 141 cases trauma or stress, including labour, were directly related to the seizure. Possibly 3 types of dissecting aneurysm are distinguishable, all based on degeneration of the tunica media. In the first medial necrosis alone is responsible. To this is added in the second type a rupture, possibly of elastic tissue, due to trauma or to hypertension continued or transitory. The third type is due to developmental defects, notably coarctation, with which degeneration of the tunica media is usually concomitant. Degrees of narrowing up to actual coarctation were found in nearly one-third of the group under 40 years. In the 24 pregnant cases the altered blood lipids of pregnancy were suspected to have caused medial degeneration. The mechanism of formation suggested is the development of a haematoma in the degenerate tunica media succeeded, although not invariably, by rupture of the overlying intima, which enables the pressure of the aortic column of blood to accelerate dissection. Since the intima is sometimes found to be intact an atheromatous ulcer is not the starting point, as has been suggested. Death ensues from rupture into the pericardium or more rarely the pleura. If death is delayed, congestive cardiac failure may be the final stage.

Peripheral aneurysm

General discussion

Aetiology.—Forty-two intracranial aneurysms which occurred in 36 individuals are analysed by Mitchell and Angrist. Twenty-two aneurysms, which conformed to the berry type, were found at the bifurcation of the basal arteries, 6 were arteriosclerotic, 2 were syphilitic and one was traumatic. For 11 aneurysms of bacterial origin the *Streptococcus viridans* from infective endocarditis, the *Staphylococcus aureus* and the *Haemophilus influenzae* were responsible. Of the arteries which form the circle of Willis the middle cerebral artery provided 10 instances of aneurysm, the anterior communicating artery 8 and the anterior cerebral 6. The internal carotid artery and arteries of the convexity were affected in 5 cases each. Aneurysms of the convexity were invariably bacterial in origin. Eight aneurysms were situated in the basilar, vertebral, posterior communicating, posterior cerebral and anterior inferior cerebellar arteries. As a general cause of rupture hypertension was significant in 9 of the 16 patients for whom clinical data were available. The local cause of aneurysm and its rupture

in the bacterial group, in the 2 syphilitic cases and in the case of traumatic arteriovenous aneurysm was necrosis of the arterial wall including the elastic fibres, which in the cerebral arteries are confined to the tunica intima. In the arteriosclerotic group the degeneration which led to rupture sometimes was general and sometimes was confined to the cerebral arteries. In the berry group, arteriosclerosis localized to the aneurysm was unexpectedly common and although defect of the tunica media was the more obvious, disruption of the elastic fibres was suspected. The latter, according to most authorities, is essential to aneurysm development. Clinical manifestations included coma, convulsions, headache, stiff neck, hemiplegia, vomiting and diplopia. Death supervened invariably within 10 days.

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ANGINA PECTORIS AND CORONARY THROMBOSIS

See also B.E.M.P., Vol. I, p. 547; and Cumulative Supplement, Key No. 62.

Angina pectoris

Aetiology

Thiocyanate sensitivity.—Odel and Horton draw attention to the toxic symptoms which may complicate thiocyanate therapy for hyperpiesia; they quote 3 cases in which angina pectoris developed as a manifestation of sensitivity to the drug. No means of preventing such toxic effects are at present known. Of the 3 patients one was a woman aged 38 years with a blood pressure of 210/130. Apart from mild retinitis no abnormal physical signs were noted. She responded satisfactorily to medical treatment, and double lumbar sympathectomy was then carried out in two stages. The blood pressure after a transient fall resumed its former level and headaches persisted. The patient attempted to take potassium thiocyanate on several occasions, but each time after 2 or 3 days vomiting developed, with dermatitis, dyspnoea and substernal pain on effort. Six months later the patient was admitted to hospital and a course of thiocyanate, 0.29 gramme daily, was begun. When the concentration in the blood reached between 1 and 2 milligrams per 100 cubic centimetres a skin eruption, dyspnoea and anginal pain developed. The drug was discontinued. After treatment with histamine diphosphate, of which 2 intravenous injections were given, the patient was able to resume taking thiocyanate, which was given in combination with histaminase by mouth. She was however obliged to discontinue the use of thiocyanate a year later because of recurrence of symptoms. In the other 2 patients, men of 48 and 51 years of age respectively, anginal attacks also developed after potassium thiocyanate was taken and in each case administration of histamine enabled thiocyanate treatment to be resumed.

Clinical picture

Report of physiological tests.—Altschule investigated the general cardiovascular dynamics in patients with severe angina pectoris, uncomplicated by congestive failure, cardiac arrhythmia or valvular disease. Twenty-two patients were studied, under basal conditions. Six are reported on in detail. The acetylene and the ethyl iodide methods were used in order to measure the cardiac output, each in half of the conditions reported on in detail. The basal metabolic rate and the arteriovenous difference were measured and the minute volume output of the heart was determined. The vital capacity, the circulation time and the venous pressures were also estimated. It was found that the cardiac index was within the normal range of 2.2 ± 0.3 litres per minute per square metre of body surface in 5 of the 6 cases studied in detail. The arteriovenous oxygen difference and venous pressures were within normal limits in every case. Values for circulation time were within the normal range in all but 5 of the 22 patients. The blood pressures were at or above 150/90 in about half the number of cases. In most instances the elevations in blood pressure were slight. A decrease in vital capacity, usually slight, was found in all instances but one in the whole series. It is concluded that a valid generalization based on physiological data constitutes a reaffirmation of the clinical concept that factors which increase cardiac work or decrease myocardial oxygenation lead to angina pectoris in patients with disease of the coronary arteries or their ostia, although reflex mechanisms are also of importance in many patients.

Course and prognosis

Duration of life.—White, Bland and Miskall report on a 'follow-up' survey of 497 cases of angina pectoris, which had been first observed at least 14 years before; it was undertaken in order to obtain more precise data concerning the prognosis. The group included 377 males and 120 females. The average age at onset was 56.5 years. The total number of those who had survived for 14 or more years was 52. Of the 445 who had died 340 were males and 105 females. The number of deaths from cardiac causes, including angina pectoris, myocardial infarction and congestive heart failure, was 340, or 76 per cent. The remaining 105 deaths were due to intercurrent disease or to injury. One hundred patients died within 3 years of the onset of symptoms; when this group was compared with the group of 52 survivors in respect of hypertension, myocardial infarction, cardiac enlargement, abnormal heart sounds, congestive failure and abnormal electrocardiograms, it was found that all these factors had occurred much more frequently among the 100 deceased patients. For example, none of the 52 survivors had shown congestive failure at the first examination, whereas it was present in 22 per cent of the others. The survivors showed a larger proportion of very nervous subjects than did the dead, whence it appears that nervous sensitivity may act

protectively by restraining the patient from over-exertion. Angina pectoris of the decubitus type seems not to be incompatible with long life.

Treatment

Failure of testosterone treatment.—The results obtained by the use of testosterone propionate in 19 cases of angina pectoris are recorded by Levine and Likoff. Sixteen of the patients were men. Nine patients had persistent hypertension and 3 gave a history of coronary thrombosis. One woman, aged 39 years, suffered from rheumatic aortic stenosis with insufficiency. The duration of angina pectoris in the whole group ranged from one month to 13 years, the average period being 6 years. All the patients used nitroglycerin for the relief of the pain. The injections of testosterone propionate were given during the autumn and early winter when anginal symptoms are often severe. Ten weekly injections of 25 milligrams were given; in 18 cases treatment was continued for 4 weeks and in one case injections were given for 7 weeks. The results of treatment were judged according to the amount of exercise the patient could take without suffering from an anginal attack and the number of nitroglycerin tablets that were taken daily. Considerable improvement was noted in 5 of the patients, that is they were able to reduce the number of nitroglycerin tablets by two-thirds of the normal amount. Two however relapsed within 6 or 8 weeks. One did not obtain any relief when given further injections of testosterone propionate. Moderate improvement occurred in one case in which aminophylline was given concurrently with the testosterone injections. Two patients reported doubtful results and in 11 cases no changes were observed. There was not any apparent effect on the blood pressure or on the electrocardiogram, and no toxic reactions were seen. It is considered that the use of testosterone propionate in angina pectoris caused no appreciable improvement, since in any case of the disease spontaneous variations in symptoms are often noted, with characteristic periods of remission.

Evaluation of methods.—The clinical evaluation of the efficacy of treatment in angina pectoris is extremely difficult and unreliable (Riseman). Various factors both physical and psychological cause patients to differ in their response to the same type of therapy and various methods of treatment obviously differ considerably in value. Furthermore, nothing short of almost complete cessation of the attacks over long periods can be regarded as a favourable response, for attacks may disappear spontaneously without any relation to treatment. Objective studies of the value of treatment in angina pectoris were made over a 10-year period in a special clinic of the Beth Israel Hospital, Boston. By using standardized exercise tolerance tests under constant conditions in such a manner as to ensure that response to therapy was the only variable factor, it was found that the value of any form of treatment can be determined objectively by measuring the amount of work that can be done before an attack of angina is induced. Electrocardiographical evidence was found to be of additional assistance. Sixty-eight methods of treatment were evaluated. Of these 20 were found to be of considerable value and 22 of slight value. The remainder were of psychological value only. A striking response to practically all available forms of treatment occurred in 27 per cent of the patients and a moderate response occurred in 33 per cent but the remaining 40 per cent failed to show any appreciable improvement. Few patients required surgery, although total thyroidectomy proved of considerable value in selected cases and the paravertebral injection of alcohol produced symptomatic relief in others.

Coronary thrombosis

Treatment

Surgical revascularization of the heart.—Beck discusses the value of operative treatment of coronary disease of the heart. The cases suitable for operation are, in his opinion, those of early disease with slight irreversible destruction of myocardium. By some thousands of experimental operations on animals he established the possibility of revascularization of the heart by grafting on it various tissues and by causing inflammation of its surface by suitable agents. Thirty patients were operated on under nitrous oxide anaesthesia. After exposure the parietal pericardium was roughened by special burrs, and powdered asbestos 0.5 gramme was applied to the heart and mediastinal fat was brought into contact with it. The patients who recovered from the operation were relieved from pain altogether or in part, and reports from 14 of them, obtained after post-operation periods ranging from a few months to 8 years, show that 7 are able to work and enjoy life. One patient, who was able to work after operation and who felt much better, died of cerebral haemorrhage after 2 years and 3 months. Post-mortem examination of the heart showed a number of vascular communications between heart and grafts.

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Odel, H. M., and Horton, B. T. (1943) *Proc. Mayo Clin.*, **18**, 279.

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ANGIOMA

See also B.E.M.P., Vol. I, p. 577; and Cumulative Supplement, Key No. 64.

Treatment

Surgery and freezing

Excision of giant naevus of the thigh.—Pickrell and Clay report on a case of a child aged 6

in whom a giant naevus of the thigh was excised and the defect successfully covered by split thickness grafts. The lesion extended from the fold of the buttock to mid-calf and was 19 inches long by 10 inches wide. The defect after excision measured 220 square inches. Only subcutaneous tissues were involved. Heavy split thickness grafts were taken from the posterior surface of the body with a Padgett dermatome. The sheets of skin were sutured to one another and to the periphery and were scored in many places in order to allow escape of exudate. A sulphadiazine film was applied to both donor and recipient areas. Healing was by first intention and the child was ready for discharge 6 weeks after operation. Microscopically, the basal epithelial layers showed moderately increased pigmentation. Mole cells were scattered through the dermis and were arranged in dense nests in the deeper layers. This is probably the largest naevus that has been excised in which the defect has been closed by grafts. Most cases of giant naevi are reported as medical curiosities. No treatment save excision with primary closure and skin grafting is apparently of lasting benefit. In the reported cases the naevi were generally present at birth and heredity was not a prominent factor, although in this case the child's father had a pigmented naevus of the buttock. In many cases there was segmental distribution but this did not always coincide with nerve distribution. Other malformations and the association of epilepsy in persons having a naevus may not be more than coincidence.

Radiation therapy

Importance of early treatment.—In the opinion of Miescher, who has treated 562 cases, irradiation therapy is the treatment of choice for angiomas, whether of the flat or the projecting type. Various forms of treatment, including the use of radium by surface or interstitial application, thorium X, Grenz rays and ordinary X-rays, are available. The author's results show that whatever method is used success depends upon early treatment, and, with flat naevi, on a comparatively limited superficial extent of the lesion. With careful adjustment of dosage damage to the skin seldom occurs. As a general rule the best method for each type of naevus appears to be as follows. (1) For flat angiomas, Grenz rays or thorium X. The former cured 36 out of 50 cases in children under a year old but failed in all of 10 cases in older people. Thorium X cured 14 out of 20 patients in the early group, but failed partially or completely in all of 19 cases in the late group. (2) Of 330 patients with projecting angiomas treated with radium 82.2 per cent were completely or almost completely cured. X-ray therapy by Chaoul's method resulted in complete or almost complete cure in 85.2 per cent (102 patients treated). Combined application of radium and X-rays cured 34 out of 44 patients.

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ANTENATAL CARE

See also B.E.M.P., Vol. I, p. 601; and Cumulative Supplement, Key No. 68.

General medical examination

X-ray examination

Screen examination as substitute for miniature radiography.—As a substitute for miniature radiography, at present unattainable for mass investigations, Frank and Jacobs employed screen examination with satisfaction in the antenatal clinic of Paddington Hospital, London. A session of 45 minutes sufficed for screening 30 persons. When abnormalities were detected, excluding minor calcified glands or Ghon foci, full-sized films were requisitioned. Of such 63 were necessary in 1,125 screenings during one year but 22 cases were later eliminated as normal. The remainder showed 6 instances of active tuberculosis, 2 of doubtful activity and 9 of quiescent or questionable tuberculosis. Calcification shadows numbered 11. The non-tuberculous conditions found included generally or locally increased vascular shadows in 8 instances, a lung partially collapsed from causes unknown and a benign pleural neoplasm not diagnosed with certainty. Pleural adhesions and a costal anomaly accounted for the remaining 3 cases. Thus 0.5 per cent required admission to hospital and 1.0 needed observation. These figures correspond with the percentage of 0.6 which required immediate or later institutional treatment and 0.4 which required observation, as shown by miniature radiography of 30,000 members of the Women's Auxiliary Air Force.

Hygiene of pregnancy

Diet

Effect of supplementary feeding.—An experiment carried out in some of the special areas of the north of England and South Wales during the years 1937 and 1939 is described by Balfour. The work was designed to test the effect of supplementing the diet of expectant mothers upon the number of still-births and deaths within the first four weeks of life, upon the rate of maternal mortality and upon the incidence of toxæmia of pregnancy. The women, selected from among those who attended antenatal clinics, were from the poorest families and a group of controls similarly selected also contained many of the very poor. The group which received the supplementary allowance included 2,465 primiparae and 9,153 multiparae, a total of 11,618; the control group included 3,352 primiparae and 4,743 multiparae, a total of 8,095. Analysis of the two groups showed that although they were not strictly comparable the inequalities were such as to weight the scales against the fed group, so that the favourable results observed can fairly be attributed to the supplementary feeding. The supplement consisted of 2 pounds of ostermilk and 1 pound of ovaltine or colact (dried

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milk flavoured with chocolate powder) together with 8 ounces of either marmite or minadex, per month. It was estimated that each woman's daily allowance represented 240 international units of vitamin A and 2,250 international units of vitamin D as well as calcium, phosphorus and iron. The results were as follows. The still-birth and neonatal death rate per 1,000 was 59.6 in the fed group and 73.3 in the control group, a difference of 13.7 per cent (minimum difference statistically significant 8.1); deaths and toxæmia cases in both groups were too few to allow any conclusions to be drawn.

Plasma content of vitamin C.—Lund and Kimble discuss the influence upon plasma vitamin C content of pregnancy, labour and diet, of the seasons and of hyperemesis gravidarum. Their studies were carried on throughout a 2-year period which included a pregnancy and labour. Determinations were carried out in 197 women of whom 43 were observed on 3 or more occasions. The woman's diet was classified at each visit as adequate, fair or poor. It was found that the vitamin C level of the blood was closely related to the type of diet, the mean values for the three groups being 0.95, 0.52 and 0.18 milligram per cent. The season exerted a considerable influence upon the diet and therefore upon the vitamin C levels. During the summer months only 7 per cent of the women were placed in the poor diet class and 64 per cent in the adequate diet class; during the remainder of the year the respective figures were 20 and 43 per cent. The results obtained did not suggest that the demand for vitamin C increases materially as pregnancy advances. The blood levels did not change during labour. A slight fall was observed during the early puerperium, especially after delivery by caesarean section. Hyperemesis gravidarum led to severe depletion of vitamin C; in some cases signs of scurvy appeared. Determinations carried out on blood from the umbilical cord showed that the foetal level of vitamin C was always higher than was that of the mother at the time of delivery; the difference was relatively greatest when maternal values were low. This may indicate selective retention by the placenta.

Balfour, Margaret I. (1944) *Lancet*, 1, 208.

Frank, Rachel, and Jacobs, A. L. (1944) *Brit. med. J.*, 1, 394.

Lund, C. J., and Kimble, Marian S. (1943) *Amer. J. Obstet. Gynec.*, 46, 635.

ANTHRAX

See also B.E.M.P., Vol. 1, p. 629.

Morbid anatomy

External anthrax

The cutaneous lesion.—Lebowich, McKillip and Conboy have studied the clinical and pathological features of cutaneous anthrax lesions. In the cases of 3 patients who were working in tanneries, the lesions were excised and sections were examined microscopically. Smears and cultures were also examined, and a saline suspension of the culture was inoculated into guinea-pigs and into rabbits in order to produce experimental lesions. Clinically the macroscopic appearance of a mature anthrax lesion is generally very characteristic, but it may be mistaken for a rare type of gangrenous syphilitic chancre or for a gangrenous carbuncle surmounted by an eschar. The absence of true pain is a significant diagnostic sign and may be due to local axonal degeneration of the cutaneous nerve fibres. The lesion is generally localized and responds favourably to specific serum therapy although from 5 to 15 per cent of non-localized cases may end fatally. The localization of the infective process is mainly due to increased filtration of fluid through the capillary vessels into the tissues, with coagulation of the plasma and the formation of a fibrinous mesh which restrains the spread of the organisms. There is no evidence of immobilization of the bacilli by the localizing action of antibodies, and apparently no agglomeration of bacilli occurs. The absence of extension of the local inflammatory response in both human and experimental lesions may also be due to a low oxygen concentration in the subcutaneous skeletal muscle, which is unfavourable for bacterial growth. In the lesions studied there was a striking absence of phagocytosis, which may have been due to the encapsulation of the bacilli in the tissues with resultant protection against leucocytes.

Lebowich, R. J., McKillip, B. G., and Conboy, Jane R. (1943) *Amer. J. clin. Path.*, 13, 505.

ANUS DISEASES

See also B.E.M.P., Vol. 1, p. 643; and Cumulative Supplement, Key No. 71.

Pruritus ani

Treatment

Tattooing with cinnabar.—Cantor classifies pruritus ani as (1) cryptogenic and (2) secondary. The secondary causes are subdivided into (a) local rectal, (b) psychogenic, (c) traumatic, (d) allergic, (e) parasitic, (f) thermal, (g) chemical, (h) general metabolic and (i) Reflex? Therapy depends upon clinical and aetiological data. If the pruritus is mild and there is not any evidence of local or systemic disorder, ordinary hygienic measures without lotion or salve are prescribed. For local abnormality—fistula, fissure, haemorrhoids—surgery is advised. In moderately severe pruritus cases, patients may require to have local injection of oil-soluble anaesthetics. Cantor does not recommend X-ray therapy. For severe cryptogenic cases tattoo or tattoo-neurotomy is advocated. Anaesthesia for this may be local infiltration, preferably with an oil-soluble anaesthetic; from 20 to 30 cubic centimetres of solution should be injected carefully in order to prevent pooling. The perianal area is then coated with an ointment such

as lanolin or nupercainal in order to hold the dye particles during tattooing. The dye used is cinnabar (mercuric sulphide) made into a heavy paste with water, alcohol, solution of merthiolate or of procaine hydrochloride. The tattoo instrument has a speed of 3,000 vibrations per minute and has from 8 to 10 fine needles set in a single row and adjusted to penetrate to a depth of 2 millimetres. The resulting tattoo should be smooth and uniform. Tattooing with cinnabar is preferable to alcohol injection. More recently Cantor has performed a combined tattoo and subcutaneous neurotomy, which is more satisfactory than either of these alone. Low spinal anaesthesia is used for this operation.

Cantor, A. J. (1944) *Lancet*, 1, 692.

APPENDICITIS

See also B.E.M.P., Vol. I, p. 729; and Cumulative Supplement, Key No. 75.

Acute appendicitis

Treatment

A review of 4,283 appendicectomies.—Behrend, reviewing 4,283 appendicectomies, includes operations for acute and chronic appendicitis and the habitual removal of the appendix when operating for other abdominal conditions. In adults physical examination aided by blood counts usually affords straightforward diagnosis. In children flexion of the thigh in response to abdominal examination is a reliable sign of inflammation. The age of the patients studied ranged from infancy to 80 years but the period from 10 to 30 years of age covered three-fifths of the operations. Haematogenous infection—often of tonsillar origin—circulatory obstruction from faecoliths, foreign bodies or anatomical deformity, and indiscretions in diet account for many cases but a universal cause cannot be assigned. The McBurney incision may be preferable when the surgeon operates for chronic appendicitis but its advantages over the direct incision, especially in reducing mortality, are disputed. The use of sulphonamide drugs in such inflammatory conditions has many successes to its credit but the sulphonamides must be regarded as still on trial. Immediate appendicectomy should be carried out after diagnosis of appendicitis. Drainage of an abscess without removal of the appendix is justifiable only in longstanding cases where nature has amputated the appendix. Increased experience has led to the reduction of drainage, which Behrend now restricts to severe infections resulting from perforation. All drainage is stopped at the end of 5 days. General anaesthesia is allowable for chronic appendicitis and ether is the anaesthetic of choice for children; in acute appendicitis spinal anaesthesia is preferable. In 2,459 acute cases 1.34 per cent was the mortality rate.

Behrend, M. (1944) *Amer. J. Surg. N.S.*, 68, 90.

ARRHYTHMIA

See also B.E.M.P., Vol. II, p. 10; and Cumulative Supplement, Key Nos. 78–85.

Tachycardia

Paroxysmal tachycardia

Use of mecholyl.—Morgan describes the treatment of paroxysmal supraventricular tachycardia, with special reference to the use of mecholyl. Although paroxysmal tachycardia is a common functional heart disorder which occurs at all ages and usually without danger to life, deaths have occurred, and hemiplegia and gangrene have followed attacks as thrombotic sequelae. The psychological factor, always more or less present, requires appropriate treatment; for the rest various forms of treatment have been found to be successful in preventing or cutting short attacks. Bromides, digitalis, quinidine by mouth, ocular and carotid sinus pressure, postural change and the induction of vomiting are severally effective in most cases. For intractable cases or those in which the heart is becoming weakened, the subcutaneous injection of mecholyl (acetyl- β -methylcholine chloride) is advocated. Oral administration is ineffective and intravenous injection should never be used as the action of the drug is rapid and dramatic when it is given subcutaneously. In less than a minute there is extreme flushing, profuse sweating and salivation and active audible peristalsis. The average dose for adults is from 20 to 50 milligrams dissolved in 1 cubic centimetre of sterile distilled water. The patient should be recumbent, with a blood pressure cuff loosely applied to an arm with easily accessible veins, and the mecholyl should be injected subcutaneously below the cuff. As soon as the heart rate and rhythm become normal the cuff is inflated to prevent further absorption. Atropine abolishes the effects of the drug and a syringe containing $\frac{1}{10}$ grain in solution should be ready for immediate intravenous injection if required on account of excessive action. The return to the normal heart rate after mecholyl injection often occurs very quickly, sometimes within 80 seconds. If an effect is not manifest after 30 minutes another dose may be given.

Bradycardia

Auriculo-ventricular block (heart-block)

A clinical survey.—Campbell discusses 64 cases of heart-block, mostly complete, which were seen during the same period as 29 cases with dropped beats and 140 cases with latent heart-block. Complete heart-block is most often seen in men in the seventh decade with enlarged hearts and atherosclerosis but no other evidence of gross heart disease. Men accounted for four-fifths of the number of patients. Nearly half the number of the patients were between 60

and 69 years old, and the great majority were over 50 years at the onset of complete block. Syphilitic and rheumatic heart disease were responsible for only one-tenth of the cases, and congenital heart disease for one-eighth. Other myocardial disease was responsible in 75 per cent. Half the number of cases showed cardiac enlargement without any other signs than atherosclerosis of the aorta and often of the peripheral arteries, and the other half showed high blood pressure, angina pectoris or congestive failure. In the 10 hyperpiesia cases the average pressure was 225/108. The heart rate was usually between 28 and 40; in the congenital cases it was generally between 40 and 56. Campbell suggests that paroxysmal heart-block should be used as a clinical term when a normal heart rate with or without latent block is the usual rhythm and heart-block the occasional finding. He distinguishes a paroxysmal heart-block (complete) when the P-R interval is normal in the interval, from paroxysmal complete heart-block when there is a latent block in the interval. Complete heart-block is a serious lesion, although some patients, especially those under 40, live for many years in reasonable health. Of 50 cases which were observed or traced for more than 2 years or until their death, 34 were dead after an average period of 2.5 years, and 16 were alive after an average period of 6 years. Of the 34 dead, 19 died in less than 2 years, 14 in from 2 to 6 years, and one after 12 years. Of the 16 alive, 10 were watched for from 2 to 6 years and 6 for from 7 to 20 years. Adams-Stokes attacks were present in half the number of patients with complete heart-block, and often appeared as an early symptom. These attacks were not more common in those who had recorded latent heart-block than in those without it. A known change of rhythm at times other than those of the attacks makes Adams-Stokes attacks more likely. The prognosis was much worse in those with Adams-Stokes attacks, and the mode of dying was strikingly different. Of these patients 61 per cent died suddenly; of the others only 1 died suddenly and 50 per cent died with failure. The risk to a patient with complete heart-block of the development of an Adams-Stokes attack is one which becomes progressively smaller. Adams-Stokes attacks may occur with paroxysmal heart-blocks (complete) which are short and therefore pass unnoticed. In cases without Adams-Stokes attacks, dyspnoea or attacks of faintness or dizziness were the main presenting symptoms.

Campbell, M. (1944) *Brit. Heart J.*, **6**, 69.

Morgan, P. W. (1943) *Ann. intern. Med.*, **19**, 780.

ARTERIAL DISEASE AND DEGENERATION

See also B.E.M.P., Vol. II, p. 39; and Cumulative Supplement, Key Nos. 86-93.

The mechanism of the arterial circulation

Ischaemic lesions

Pathological review.—Blackwood presents some views of a pathologist on ischaemia. Conditions primarily due aetiologically to structural abnormalities or damage are chronic arterial disease, thrombo-angiitis obliterans, traumatic arteritis, embolism, thrombosis, syphilitic and tuberculous arteritis and periarteritis nodosa. Functional abnormalities are seen in Raynaud's phenomenon and in reactions to chemical stimuli such as ergot, tobacco and carbolic. The effects of ischaemia are shown by various findings. The peripheral pulse, the skin temperature, the colour of the limb (as placed in different positions), the power to initiate or sustain movement and the nerve dysfunction are indications of the effect of ischaemia. The structural changes of the tissues supplied are discussed. There is a general atrophy of the soft tissues and of the bone, but if of sufficient degree the ischaemia will result in necrosis. Degenerative changes have been found in the nerves and are most obvious in their distal portions. Various factors modify the consequences of ischaemia. The degree of narrowing of the lumen, the site or sites of the narrowing and the extent of collateral circulation are factors governing the available blood supply. The rate at which the ischaemia develops and its duration affect the amount of adaptation to a lowered blood supply which is possible. The sharing of the blood between the tissues is stressed; anything which causes an increased flow to one area may mean a dangerous lowering of the blood flow to another area, hence reflex vasodilatation has its dangers because it allows the skin to receive blood at the expense of the muscle.

Functional disorders

Treatment

Review of peripheral vascular disease.—In peripheral vascular disease two distinct factors are at work: vasospasm and diseased processes within the vessel wall. Stammers emphasizes the importance of determining, for purposes of accurate diagnosis, prognosis and treatment, which factor predominates in such cases. It would appear that vasospasm, produced by exposure to cold, is almost the sole cause of such conditions as Raynaud's disease, acrocyanosis and the severe and sustained spasm which sometimes involves limbs previously affected by poliomyelitis. In all such cases warm environment or heat to the trunk only is generally sufficient to cause spontaneous disappearance of the blueness and coldness of the extremities and thereby establish the diagnosis. Furthermore, avoidance of cold and damp, both climatic and occupational, and adequate warm covering for hands and feet will usually prevent the onset of symptoms. Should these measures fail however preganglionic sympathectomy offers relief and sometimes complete cure. Hyperhidrosis, also, is due largely to overaction of the sympathetic nervous system. When vasospasm plays a minor part however as in cases of thrombo-angiitis obliterans or scalenus anticus syndrome, a more delicate test is necessary.

The rise in skin temperature of the affected limb which occurs after the induction of an artificial pyrexia with T.A.B. vaccine or, in the case of the lower limb, during spinal anaesthesia, will show roughly to what extent vasospasm is responsible. Cases of thrombo-angiitis obliterans (Buerger's disease or juvenile gangrene) often benefit by treatment with pressure pulsators, contrast baths, and injections of some vasodilator (for instance a pancreatic vasomotor hormone such as padutin) or by the mild pyrexia produced by weekly injections of T.A.B. vaccine. Preganglionic sympathectomy is efficacious only in young subjects in whom the element of vasospasm is considerable. In cases of scalenus anticus syndrome, scalenectomy, with excision of the cervical rib or of the fibrous band when present, is the only rational treatment.

Acute arteritis

Clinical picture

Localized arterial thrombosis in young adults.—During the past 2½ years Learmonth, Blackwood and Richards have studied the vasomotor reactions in 4 cases of localized arterial thrombosis in young adults. In 2 of the cases they made histological examination of the affected artery. The result of this indicated, by a process of exclusion, that trauma was a causal factor. One case was that of a naval rating, 25 years of age, who had spent 4 or 5 hours in the water after being torpedoed. Later he had a similar experience. As a result he had acute phlebitis of the right foot and leg and vasomotor changes in the right hand. As the condition grew worse the brachial artery was tied, and also the radial and ulnar arteries, and the obstructed portion of the vessels was removed. The lumen of the thrombosed artery contained an organized thrombus with small blood vessels running across it. The 3 main arteries showed damage to their inner and muscular coats. The index finger, which had to be amputated, showed similar changes in its blood vessels with marked crenation of the elastica. An accurate diagnosis can be made by examination of the peripheral pulses, by noting the response to reflex vasodilation and by arteriography. Treatment should be directed towards the provision of the best collateral circulation and the prevention of spread of the thrombus. The procedure of preganglionic sympathectomy will ensure the former. With regard to the latter, if arteriography shows that the blocked portion is large and that the thrombus is approaching collateral vessels, arteriectomy is indicated.

Periarteritis nodosa

Clinical picture

A new syndrome.—MacKeith describes 3 cases of polyarteritis (periarteritis) nodosa which showed what he believes to be a new syndrome—localized soft pitting oedema of the skin of one or more limbs together with asymmetrical muscular weakness. In all 3 cases the diagnosis was confirmed by biopsy. The first patient was 27 years of age, and had oedema of the right upper arm and weakness of the right arm and thigh. He recovered. The second was aged 63 years and had oedema of the ankles and legs, elbows and right thigh, with left wrist-drop. He died 2 months after admission to hospital. The third patient, aged 58 years, had oedema of elbows, forearms, ankles and lumbar region, with right wrist-drop. He recovered after 6 months' treatment. All 3 patients had leucocytosis but not any eosinophilia. There was increased plasma albumin in 2 cases which were tested. This finding may be of diagnostic value. Skin nodules were present in one case only. Treatment consisted in rest, high vitamin diet supplemented by injections of vitamin B₁ and splinting and massage for the limbs. Another case showed a similar clinical picture and increased plasma albumin, but 2 biopsies were negative for periarteritis nodosa.

Blackwood, W. (1944) *Edinb. med. J.*, **51**, 131.

Learmonth, J. R., Blackwood, W., and Richards, R. L. (1944) *Edinb. med. J.*, **51**, 1.

MacKeith, R. (1944) *Brit. med. J.*, **1**, 139.

Stammers, F. A. R. (1944) *Med. Pr.*, **211**, 308.

ARTHRITIS: RHEUMATOID ARTHRITIS

See also B.E.M.P., Vol. II, p. 74; Interim Supplement, No. 19*; and Cumulative Supplement, Key No. 98.

Clinical picture

Arthritic period

Metabolism in arthritis.—Ropes, Rossmeisl and Bauer have studied the calcium, phosphorus and nitrogen metabolism in 9 patients with rheumatoid and 3 with degenerative arthritis. Each patient was placed on a constant diet low in calcium. Urine and faeces were collected in 3-day periods. Serum calcium and phosphorus were normal in all the cases. Serum phosphatase was within normal limits except in 2 cases in which it was raised. Calcium excretion was slightly raised in the patients with rheumatoid arthritis and decreased in those with degenerative disease. The rate of calcium metabolism was slightly increased in the former group. No other abnormalities were noted.

Pathology and prognosis

Comparison with osteoarthritis

Surgery and chronic arthritis.—Colonna reviews the part played by surgery in the evolution of the treatment of chronic arthritis, which has assumed progressive importance during

the last 10 years with the more careful selection of patients for the improved technique of joint surgery. The cases of chronic arthritis are divided on pathological rather than on aetiological grounds into two main groups: (1) rheumatoid, proliferative or atrophic and (2) degenerative, osteoarthritic or hypertrophic. Nichols and Richardson first published a careful laboratory study based on necropsies. The proliferative form primarily involves the soft tissues around the joints and occurs predominantly in the first four decades of life; the smooth, glistening joint surfaces are gradually encroached upon by a pannus formation of granulation tissue, which follows the pattern of an inflammatory process. Ultimately the joints often undergo bony ankylosis. The other, the degenerative, form is in distinct contrast, and is essentially a process of tissue degeneration; the articular cartilage early shows a yellow hue and fibrination. The weight-bearing portions of the articular cartilages undergo attritional change with eburnation of the opposing joint surfaces and lipping of the marginal areas of the joint; the degeneration appears first in the portions most subject to the pressure and strain of weight-bearing. The changes are ascribed to repeated trauma to tissues that have not the power of withstanding them. There is a restriction to motion but no bony ankylosis. The orthopaedic surgeon should be chiefly responsible for the prevention of deformities and for the correction of any joint deformity that has appeared. Physical treatment is one of the most important measures, especially in the degenerative form. If the deformity has become severe or is of long standing, its correction may be best obtained by careful manipulation under anaesthesia with frequent changes of external support during the period that the periarticular tissues are undergoing stretching and relaxation. It is usually advisable therefore to precede any surgical intervention by proper splinting and corrective muscle-training exercises. Deformities in chronic arthritides can be treated by many valuable non-surgical measures, but within recent years this kind of patient has also been able to receive positive benefit from operation. The hip joint and the knee joint are given as examples, and arthroplasty is recommended for an ankylosed or partially ankylosed hip. The operation of synovectomy of the knee has proved to be of great value in chronic arthritis of the knee.

Treatment

General

Importance of early treatment.—The management of early rheumatoid arthritis is described by Bach. The rheumatoid type of arthritis is not the most common rheumatic condition seen in medical practice but it causes a greater degree of crippling than does any other rheumatic disease and it has more need of early institutional treatment. It is a systemic disease of undetermined origin but there is evidence that infection may be an important causal factor. Some sufferers become gradually crippled in spite of every medical care but in others the disease can be arrested before there is much crippling even if treatment is inadequate or lacking altogether. In the majority of patients however early and adequate treatment is essential to prevent gross disability. In the early stages it may be difficult to make the diagnosis on clinical signs alone and investigations such as a blood count or a blood sedimentation test may be necessary. The author outlines the treatment given when the patient is admitted to hospital for routine investigations. The first principle of treatment is rest. The uses of bed exercises are explained to the patient. Deformities must be corrected and serial plasters may be required. General irradiation with a mercury vapour lamp and ionization applied to the affected joints and reciprocating faradism to the wrist and thigh muscles, are beneficial. Various forms of support may be advisable in order to correct faulty posture and to strengthen the feet. Drugs and liniments are used to relieve pain and stiffness. Liver extract, iron and vitamins B and C are prescribed and insulin and hydrochloric acid may be indicated in some cases. Stilboestrol should be used in menopausal cases and gold may be of great help if the sedimentation rate is raised. The diet should have a high caloric value with a relatively high protein and fat content and should be reduced in carbohydrates. As the patient progresses class exercises and remedial rehabilitation therapy are included in the scheme of treatment. The aim is to help the patient to increase his physical resistance by altering some of the constitutional and environmental factors which lead to ill health.

Medicinal

Chrysotherapy.—Cohen and Dubbs describe the results obtained in a group of 122 patients with rheumatoid arthritis who were treated by injection of gold salts. Gold therapy is practically the only method of treatment of arthritis that has given consistently favourable results but its use has been limited because of the associated risk of toxic reactions. In the above series aurothioglucose (solganal B oleosum) was given intramuscularly with a maximum dosage of 1.24 milligrams in 15 weeks. A second course of injections was given after an interval of 6 weeks unless a patient had experienced untoward reactions. Most of the patients had severe rheumatoid arthritis and the usual investigations were carried out. Sedimentation tests were made after each course of injections and blood counts and urine analysis were made weekly. Each patient took 16 fluid ounces of fruit juices and at least a quarter of a pound of liver 3 times a week, because it was considered that, if the capillary permeability of the mucous membranes was decreased by a supplementary intake of vitamin C, the incidence of untoward effects might be reduced. If such reactions occurred, either mild or severe in type, the gold treatment was suspended and intramuscular injections of crude liver extract were given. Of the 122 patients reactions occurred in 12 who received one course of treatment, in 38 who received 2 courses and in one out of 16 who had 3 courses. Thirty-five per cent of

the patients in the whole series showed only subjective improvement, 17 per cent were considerably relieved, 9 per cent did not experience any relief and 4 per cent appeared to be worse after treatment. It is not known whether or not a gradual reduction in the sedimentation rate is related to the rate of improvement in any case. It is concluded that advanced age is not a contra-indication to gold therapy. In the authors' cases the unfavourable reactions were comparatively few, possibly on account of the prophylactic and precautionary measures taken.

Certain authorities claim a success rate of nearly 80 per cent when rheumatoid arthritis is treated with gold, but dangers, and even a 1 per cent mortality, are to be apprehended. Graham and Fletcher, recounting experiences with 100 patients, emphasize the dangers. Fifty-four patients showed a total of 70 toxic reactions, of which 4 instances of exfoliative dermatitis gave most anxiety. It is however remarkable that severe general reactions coincide with dramatic articular improvement. Mild skin reactions, ulcerations of mucous membranes and gastro-intestinal disturbance to a total number of 43 yielded to immediate temporary pre-emption of gold administration. Of renal symptoms, occasional traces of albumen are insignificant but albuminuria with erythrocytes or casts in 7 patients indicated that treatment had to cease. In 8 cases transitory reaction in joints to each injection did not interrupt treatment. Leucopenia, the only haemic deterioration observed, caused cessation of treatment in the case of 4 patients. A central scotoma which cleared in 3 months and 3 cases of lost sense of taste and of smell were the only disturbances of the central nervous system. Sodium aurothiomalate (myocrisin) in an aqueous solution containing 50 per cent of metallic gold was injected intramuscularly. A course—3 courses may be necessary—consisted of 2 small test doses a week apart and afterwards weekly doses of 0.10 gramme for 10 weeks, totalling 1.06 grammes. The essential safeguards are a weekly leucocyte count, analysis of urine and estimation of sedimentation rate. The magnitude of fall in sedimentation rate was exactly correlated with the benefit received. Omitting 5 patients whose toxic reactions compelled permanent cessation of treatment, the results attained were in 64 patients remission or great improvement, in 19 improvement and in 12 not any improvement. Pregnancy, hepatic or renal disorders and cutaneous diseases contra-indicate gold treatment and its use in articular disease must be confined to rheumatoid arthritis.

Review of chrysotherapy.—Price and Leichtenritt have reviewed a series of 101 patients who were treated for rheumatoid arthritis with gold salts. The patients, of whom 52 were male and 49 female, were classified in three groups as follows. (1) The mild group included 14 cases in which the disease was mainly confined to the periarticular tissues and little or no sign of bony change was seen in the X-ray film; all but one of these patients were ambulatory. (2) The moderately advanced cases, 30 in number, showed more extensive joint disease, with destruction of cartilage and limited ankylosis in some of the patients, of whom 8 were bedridden. (3) The severe group comprised 57 patients with multiple arthritis, extensive ankylosis and deformity. Radiograms showed decalcification of the bones of one or more joints and loss of the intra-articular space; 90 per cent of the patients were bedridden. The gold preparations used were myocrisin for 91 patients, solganal B oleosum (aurothioglucose) for 10. The dosage varied during the period covered by the report. During the earlier years covered by the report weekly doses of 100 milligrams were given for from 18 to 20 weeks; subsequently this dose was given twice weekly. In 1940 the dose was reduced to 50 milligrams and later to 25 milligrams once or twice weekly. Solganal B oleosum was given in initial doses of 10 milligrams twice a week, increased gradually to 100 milligrams. A single course of treatment was given to 40 patients; the remainder received from 2 to 6 courses with intervals of from 2 to 6 months between the courses. Some form of toxic reaction occurred in 38 per cent. The results were: (1) in the mild group 13 improved and 11 maintained improvement; (2) in the moderate group 24 improved and 18 maintained improvement; (3) in the severe group 23 improved and 13 maintained improvement. The authors are convinced of the value of aurotherapy for rheumatoid arthritis, especially for early cases, but consider that its use should be limited to this type of rheumatic disorder.

Bach, F. (1944) *Practitioner*, **152**, 20.

Cohen, A., and Dubbs, A. W. (1943) *New Engl. J. Med.*, **229**, 773.

Colonna, P. C. (1943) *Trans. Coll. Phys. Philad.*, 4th Ser., **11**, 1.

Graham, J. W., and Fletcher, A. A. (1943) *Canad. med. Ass. J.*, **49**, 483.

Price, A. E., and Leichtenritt, B. (1943) *Ann. intern. Med.*, **19**, 70.

Ropes, Marion W., Rossmeisl, Elsie C., and Bauer, W. (1943) *J. clin. Invest.*, **22**, 785.

ARTHRITIS: OSTEOARTHRITIS

See also B.E.M.P., Vol. II, p. 91; and Cumulative Supplement, Key No. 100.

Treatment

Methods of physical medicine

Therapeutic review.—Among the many confused forms of rheumatic affection, rheumatoid arthritis and osteoarthritis are outstanding types which can be easily distinguished. Ray contrasts the early appearance of osteophytes, the late erosion of cartilage and the coarse skin in osteoarthritis with the opposite occurrences and glossy skin of rheumatoid arthritis. The raised erythrocyte sedimentation rate of rheumatoid arthritis contrasts with the normal

rate of osteoarthritis and the average age of onset in the latter case is later by 20 years. Osteoarthritis attacks mainly the articular lamella of compact bone, the articular cartilage and the synovial membrane. Radiography is invaluable in diagnosis. Heredity, the climacteric age involving obesity and endocrine influences and trauma including persistent stress are causative agents. Focal sepsis is not responsible. The occupational arthritis in elbow and shoulder of blacksmith and plasterer illustrates the effect of trauma. In women the knees often suffer at the menopause, illustrating endocrine influence and the persistent stress resulting from increased weight. Relatively, men are more often affected in the hips. The feet, hands, jaw and auditory ossicles are common sites of osteoarthritis in both sexes. In the spine osteophytes are radiographically seen in 93 per cent of persons over 60 years of age. Treatment aims at relief of pain and at prevention of deformity. Of drugs, aspirin and veganin are useful anodynes but neither of them nor any other drug is curative. Thyroid administration is adjuvant to weight reduction. Physiotherapy (to include exercises), friction and the varied forms of heat application are beneficial and counter-irritation often affords relief. A removable plaster splint permits the maintenance of a judicious balance between exercise and rest.

Surgery

Treatment of chronic arthritic deformities.—Colonna states that deformities in chronic arthritic patients, whether they are of the rheumatoid or of the osteoarthritic type, can be reduced by certain surgical operations. Surgical intervention should, however, be preceded by proper splinting and by muscle-training exercises, and operation should be delayed until the disease has been inactive for at least a year. The principles involved are discussed in reference to the hip and knee, both weight-bearing joints. In the hip joint, arthritis involves the joint cartilages, and stiffness, pain and deformity result, with loss of balanced movement and with limping. The deformity must be corrected, for a person can walk well with a perfectly ankylosed hip provided that the limb is in the attitude of election, namely slight flexion and abduction. An open operation may be necessary, one of the simplest being osteotomy. The essential feature is a division of the femur at the level of the lesser trochanter and the placing of the limb in plaster of Paris in the position of election. Immobilization is continued for from 6 to 8 weeks or until the osteotomy is united by bony union. In certain arthritic hips operation may be necessary solely for the purpose of relieving pain. In these cases arthrodesis of the joint is valuable, particularly in younger patients. In some osteoarthritic cases an increase in the local circulation of the head of the femur is obtained by the so-called drilling operation. Arthroplasty is useful in dealing with the ankylosed or partially ankylosed hip. Other possible procedures are the acetabuloplasty of Smith-Petersen, excision of the osteophytic fringe and the pseudoarthrosis operation of Sir Robert Jones. In the arthritic knee joint complete extension is lost early, and a small amount of fixed flexion can be very disabling. If conservative measures fail the joint can be manipulated under anaesthesia. Open operations such as tenotomies and capsulotomies are used. For some patients a joint which has been surgically fused in either a straight or a slightly flexed position is of more practical value than is a movable painful one. Occasionally there are multiple loose bodies in the joint which may cause mechanical locking and which require removal. In specially selected cases removal of the patella may be advisable. Arthroplasty should be considered in the case of a painless ankylosed joint with good muscular potentialities. Synovectomy is very useful for chronic arthritis of the knee with persistent thickened synovial membrane and chronic synovitis, particularly when only one knee is affected.

Colonna, P. C. (1943) *Trans. & Stud. Coll. Phys. Philad.*, 11, 1.

Ray, M. B. (1944) *J. R. Inst. publ. Hlth Hyg.*, 7, 14.

ARTHRITIS: SPONDYLITIS

See also B.E.M.P., Vol. II, p. 105.

Ankylosing spondylitis

Clinical picture

Summary of treatment.—A communication by Buckley to the East Midlands Society of Physicians, England, deals with spinal arthritis in young people. The commonest form is the Strümpell-Marie type of ankylosing spondylitis. The earliest symptoms are vague pains in the back and in the limbs; flattening of the normal lumbar curve becomes evident soon after. The pathological changes consist in (1) synovitis of the apophysial joints of the lumbar spine, which quickly spreads to the dorsal spine and to the costovertebral joints and (2) rarefaction of the bones. The sacro-iliac joints are usually affected and later the other large joints. The disease usually attacks males and possibly is related to the rapid development of the sexual glands. A rather different form is seen at a slightly later age, namely between 30 and 40 years. The disease starts in the dorsal spine; the changes are less pronounced and progress more slowly. In all cases of pain in the back in young people an X-ray photograph should be taken. If changes in the lower lumbar apophysial joints are observed and if the blood sedimentation rate is raised the diagnosis is reasonably certain. Treatment in the early stages consists of rest in bed; later, as the acute symptoms subside, the wearing of a plaster jacket. The latter should be worn for several months, after which a spinal brace should be substituted. Plenty of milk and extra vitamins should be given and heliotherapy should be applied to improve the general health and to promote calcium metabolism. Breathing exercises are important and deep

X-ray treatment is sometimes helpful. Aspirin may be given in order to relieve pain. Gold and vaccine treatments are completely ineffective in young subjects.

Buckley, C. W. (1943) *Brit. med. J.*, 2, 4.

ARTHRITIS: GENERAL

Treatment

Physiotherapeutic methods reviewed

Governing factors in the treatment of arthritis, according to Snow, are psychological status, pain and disability, prognosis and finally the patient as a whole. The methods of physical therapy advocated are moist heat, generalized heat, dry heat, massage, passive movements, rest, light, electrotherapy and exercise. Physical therapy is indicated in arthritis when it is desired to improve or preserve function and to lessen deformity and pain. From this point of view there are 6 classes of cases: rheumatic fever, septic, gonococcal and gouty arthritis, rheumatoid arthritis and osteoarthritis. Physical therapy should never be given merely for its psychological effect. In arthritis of the legs, knees and ankles the patient should be given crutches early in order to assist weight-bearing. Adequate rest must be insisted on. Diathermy applied to the affected joint gives much relief. Arthroplasty of the hip may restore hip function if physical therapy is given afterwards. Traumatic arthritis of the foot bones may necessitate the use of special supports or of orthopaedic surgery. Bivalved casts, removed daily for passive movements under water, are advocated in rheumatoid arthritis, as are exercises performed in bed.

Snow, W. B. (1943) *New Engl. J. Med.*, 229, 959.

ASCITES

See also B.E.M.P., Vol. II, p. 153.

Causes of ascites

Nutritional deficiency

Analysis of cases occurring in India.—Hardikar and Rao analyse 488 cases of ascites admitted during 2 years to the Osmania Hospital, Hyderabad. In Bombay and Delhi cardiac insufficiency greatly preponderates over hepatic cirrhosis in causing ascites whereas cirrhosis slightly preponderates in Hyderabad. The incidence of cirrhosis apparently corresponds with the greater consumption of rice in south-eastern India, contrasted with the dependence of north-western regions on *jawar* and wheat. The 488 cases comprised 327 instances of cardiac, renal and hepatic disease, 38 instances of peritoneal tuberculosis and carcinoma and 33 anaemic conditions; there were also 90 cases of indefinite causation. Such patients presented generally a picture of pronounced asthenia and variable anaemia. Nothing pathognomonic could be attributed to any organ or system. The bradycardia, enlarged heart and polyneuritis of beri-beri were absent and oliguria when present yielded readily to diuretics. On the supposition of nutritional deficiency a diet of 2,000 calories was instituted. A diuretic mixture, a dose of magnesium sulphate if required and occasionally an intramuscular injection of the mercurial diuretic neptal was the medication employed. Response to the treatment was satisfactory. Is the condition to be regarded as atypical beri-beri, famine oedema and vitamin deficiency or as early hepatic cirrhosis? The cause of the peritoneal exudate also remains undetermined but experimental injection of sodium iodide into the peritoneal cavity and its partial recovery from the urine proves that the peritoneum retains some power of absorption.

Hardikar, S. W., and Rao, V. G. (1943) *J. Indian med. Ass.*, 13, 1.

ASPHYXIA IN CHILDREN

See also B.E.M.P., Vol. II, p. 173; and Cumulative Supplement, Key No. 109.

Asphyxia during the early weeks of life

Treatment

Statistics of the intelligence quotient.—Darke finds that severe asphyxia neonatorum adversely affects subsequent mental status. The oxygen requirement of cerebral tissue is said to be twenty times that of resting muscle, and 8 minutes of anoxia suffices to cause permanent damage. Nineteen children were studied, with an age-range of from 2½ to 11 years, whose hospital records conformed to 3 requirements: (1) an absence of organic neurological findings at birth or present examination; (2) birth must have been attended by asphyxia pallida or an apnoeic period exceeding 3 minutes; (3) efforts were made to exclude any possible case of intracranial haemorrhage, with what success cannot be known. All the cases conformed to the first requirement. Group (1) comprised 10 children conforming exactly to the second criterion and group (2) comprised 4 children believed from their birth records so to conform. Group (3) comprised 5 children in whom severe asphyxia did not progress to asphyxia pallida; the duration of apnoea was not recorded. To each investigated child was allotted a parent or sibling of that child as control. The test employed was the 1937 revision of the Stanford-Binet Intelligence Scale. Group (1) gave an intelligence quotient reading averaging 87, contrasted with the average control quotient of 99.3. In group (2) the corresponding readings were 77 and 99.7 and in group (3) 98.4 contrasted with 103.4 as the control reading. In 2 cases only, one of which belonged to the least defined group (3), did the subject of

investigation surpass the intelligence quotient of the control. Measures to combat anoxia in degree and duration are outside the scope of this investigation, but the justification for oxygen administration is clear. The recently devised method of continuous caudal anaesthesia in obstetric practice, by eliminating inhalational anaesthesia, shortening the second stage of labour and reducing birth injury, may prove to be valuable in this connexion.

Darke, R. A. (1944) *J. Pediat.*, **24**, 148.

ASTHMA

See also B.E.M.P., Vol. II, p. 179; Interim Supplement, No. 17*; and Cumulative Supplement, Key No. 110.

Aetiology

Non-specific factors

The alarm reaction and its effect on the adrenal output.—Rackemann reviews facts and theories concerning asthma, and takes as a test the case of a patient in Massachusetts General Hospital who had asthma almost continuously for 5 years. For many years previously he had been subject to nasal catarrh and recently to sinusitis. He was at the time of writing in poor condition, very thin, miserable and apprehensive and unable to concentrate on anything. Three sinus operations and the extraction of 6 septic teeth had not given him any relief; an X-ray of the chest showed no organic lesion. The nervousness was manifestly a result and not a cause of the asthma. None of the ordinary theories concerning the cause and nature of asthma were applicable to this case, which did not present either allergy or toxicity, but there appeared to be evidence of abnormality in adrenal gland function. Adrenaline relieved the patient only partially. One of the functions of the adrenal cortex is concerned with metabolism of salt and water and a number of clinical observations suggest that there is a disturbance of this metabolism in asthma. In a group of 5 patients observed it was found that during the asthma attacks there was marked loss of sodium and water. Rackemann mentions experiments made by various observers which are corroborative. In Addison's disease the sodium content of the blood is low and a diet without sodium may bring on symptoms of the disease which are relieved when sodium is again given. Asthma has been treated with extract of the whole adrenal cortex, eschatin, with good effect in some cases, and administration of extra salt has been found beneficial in very debilitated patients. Rackemann suggests that severe and continuous asthma, as in this case, may be the expression of a general and diffuse physiological disturbance, the effect of an 'alarm reaction', which, according to Selye's theories, may be developed as the result of many kinds of injuries and shocks to the body.

Meteorological influences.—Petersen and Vaughan have examined the clinical course of asthmatic patients who died from the disease as related to major changes in the meteorological environment—temperature, barometric pressure and precipitation. The normal person must adjust himself to the passage of alternating tropical and polar air masses by means of the autonomic nervous system. In asthma, weather factors may be important in making an allergic patient more sensitive to his allergen or in modifying the quantitative or qualitative state of the allergen. The asthmatic patient, with his great autonomic lability, is at most times very sensitive to changes in the air mass. It is also possible that with steady exposure to an allergen of low activity for the particular patient (say, house dust) weather change might cause an acute attack. Weather change is at times a factor in tipping the balance towards a fatal outcome. There is evidence that tolerance to narcotics, including opiates, may be impaired in unfavourable weather. In the patients studied the weather change which preceded an asthmatic attack was usually that of falling temperature and death often occurred when the temperature subsequently rose. Other types of weather change may be significant such as change in humidity, air ionization and wind velocity. The important factors are abrupt or violent weather changes and the extent of the physiological adjustments in the body. In certain circumstances however similar weather changes may not affect the patient adversely. It is the combination of many factors or of all of the factors that matters—for example, allergen exposure, fatigue, infection, constipation, menstruation and weather changes.

Association with tuberculosis

Tocker and Davidson discuss the relation of bronchial asthma to pulmonary tuberculosis. Some mention is also made of the relation between hay fever and tuberculosis. The opinions most commonly expressed by previous writers are summarized as follows. (1) Bronchial asthma and pulmonary tuberculosis are antagonistic and are rarely, if ever, found together. (2) Asthma and tuberculosis may occur together but purely coincidentally and no causal relation exists between them. (3) In the majority of instances asthma is of tuberculous origin. (4) Asthma often begins as a result of allergy to the tubercle bacillus but hypersensitiveness to other allergens may develop later. (5) Asthma predisposes to pulmonary tuberculosis. (6) Asthma is favourably influenced by pulmonary tuberculosis. These varied opinions are due to the failure to differentiate between true bronchial asthma and asthma-like symptoms which are caused by various intrapulmonary pathological conditions. The authors report on 386 tuberculous patients. Each patient was carefully questioned for a past or present history of allergy in himself and in the immediate members of his family. In the case of any patient with a definite or suggestive history intradermal tests were made with the common inhalant and food allergens. Eosinophils were looked for in blood and sputum in doubtful cases. Radiological examinations were checked with the test results. Of 386 patients with active

pulmonary tuberculosis 3·1 per cent gave a past or present history of bronchial asthma and 2·8 per cent a history of hay fever. These figures are about the same as are those for the incidence in the normal population. Of the 11 cases of hay fever only 2 patients gave a history of asthma. These findings refute earlier reports that tuberculosis and asthma are antagonistic, that tuberculosis predisposes to asthma and that there is a specific form of asthma due to allergy to the tubercle bacillus. The allergens which produce bronchial asthma in patients with tuberculosis are the same as those which produce asthma among the non-tuberculous. The effectiveness of skin tests with these allergens are often however impaired as a result of diminished skin reactivity in the debilitated cases. Asthmatic symptoms tend to improve with activity of a tuberculous process and to recur with healing of the infection. Asthmatic seizures are a potential source of danger to the favourable course of tuberculosis, particularly during treatment by artificial pneumothorax.

Clinical picture

Types in childhood

The psychological aspect.—Rogerson analyses the significance of psychological factors in asthma, and suggests that psychological treatment should supplement physical treatment and should be given concurrently. In many cases of asthma in children an over-anxious and over-protective attitude is shown by one or both parents. The asthmatic child has a personality type characterized by high intelligence, irritability and aggressiveness; he is over-anxious and lacks self-confidence. He may appear submissive but generally shows signs of tension and demands constant attention. This exaggerated need leads ultimately to frustration which becomes intolerable and inescapable. Asthmatic subjects often also suffer from eczema and prurigo, showing abnormal physical sensitiveness and irritability. Their personality is a psychological expression of these traits. The symptoms of asthma may be symbolic of mental conflict; they may be the signs of anxiety or the result of a conditioned reflex or they may be the means of achieving some purpose. In most cases the asthma attack is the sign and resultant of conflict in the same way that palpitations are the result of fear. The asthmatic stands tension very badly but generally finds it necessary to continue his normal life regardless of attacks, otherwise they become much worse. The most important but least appreciated effect of the psychological factor is to render the subject more sensitive to the operation of physical factors. The physician should advise the parents to encourage the development of the child's personality so that he becomes more independent and more able to stand on his own.

A general review.—Hurst discusses asthma in childhood and various procedures of treatment. Asthma is defined as the reaction of an over-excitabile bronchial system, and the diathesis is a congenital and often inherited constitutional abnormality. There is probably also an associated psychological factor, the so-called 'asthma personality'. The asthmatic child is hyperintelligent and over-anxious and lacks self-confidence, but is often aggressive and dominating. If a child can be kept completely free from asthma for 2 years he will probably remain free from attacks for the rest of his life. Defect of the respiratory tract is the main reflex cause of asthma, and an asthmatic child should not be allowed to remain a mouth-breather on account of congestion of the nasal mucous membrane. In many cases asthmatic attacks occur after colds or acute bronchial infection, either from increased permeability of the respiratory mucous membranes to allergens or from bronchial spasm by a short or long vagal reflex. Distension of the stomach or rectum can also cause reflex attacks of asthma, but alimentary toxæmia is never responsible. The most common psychological cause is expectation, but emotions such as annoyance, excitement and anxiety are also predisposing causes. Parental anxiety may be transferred to the child, who often improves when he is away from his home influence. In the past, treatments for asthma have been many and various and have in turn been abandoned. Specific desensitization has had a more lasting popularity than has any of the earlier methods, but various workers have shown that saline solution, peptone, tuberculin and other reagents have given equally good results owing to the suggestive effect of such injections. Every asthmatic, however, can derive much benefit from good advice and by adapting his mode of life so that the exciting causes of his particular brand of asthma are avoided. Expiratory exercises help in the restoration of the normal postural tone of the chest muscles and the asthmatic child should be encouraged to join in sports. He should avoid any proved allergens; iodides, caffeine and theophylline, and adrenaline help to control attacks and minimize discomfort.

Diagnosis and differential diagnosis

The Weltmann reaction

Detection of infection or fibrosis in asthmatics.—A study of the results of the Weltmann reaction in 224 cases of bronchial asthma is reported by Dees¹, and the technique of the method is described. The group of patients comprised 51 children and 173 adults. The Weltmann reaction is a coagulation test in which serum is mixed with solutions of hydrated calcium chloride ($\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$) of varying concentrations. A series of 10 test-tubes is used, each containing 0·05 cubic centimetre of unhaemolysed serum. After the addition of the test solutions the tubes are placed in boiling water for 15 minutes. With normal serum coagulation occurs in the first 6 tubes with solutions of concentrations ranging from 0·1 per cent to 0·05 per cent. The Weltmann reaction in serum from normal adults and children therefore has a remarkably constant value, as a coagulation band of 6. Acute infection and inflam-

matory processes have coagulation bands of less than 6, whereas conditions characterized by the formation of fibrous tissue have bands greater than 6. The author's patients were classified clinically into 5 groups: (1) asthma, (2) asthma and other allergic conditions, (3) asthma with non-infective diseases, (4) asthma with chronic infections and (5) asthma with acute infections. The patients with uncomplicated asthma or with asthma and other allergic conditions had coagulation bands of 6, except 6 patients with asthma due to bacterial allergy and pulmonary infections, who all had bands of 5. The patients with non-infective complications had bands of 7 or a higher coagulation equivalent. All the patients with infection had bands less than 6, except 24 asthmatics with chronic mild infection or pulmonary fibrosis. By the Weltmann reaction it is therefore apparently possible to detect infection or fibrotic change in asthmatic subjects.

Treatment

Treatment of attacks

Use of oxygen, adrenaline hydrochloride and glycerin.—Lockey describes the treatment of bronchial asthma by the inhalation of oxygen and 1 in 100 adrenaline hydrochloride solution modified by the addition of 5 per cent glycerin. For many years various solutions of bronchodilator drugs have been used for the relief of asthma, but certain limitations and disadvantages have been encountered. Adrenaline solutions without added glycerin often cause dryness and irritation of the throat, nervousness, palpitation, nausea, headache, dizziness and weakness. Sixty asthmatic patients were divided into two groups for the purposes of study. The first group used 1 in 100 adrenaline solution by inhalation from a hand bulb vaporizer, and the second group used the same solution with 5 per cent of glycerin added. Both groups recorded their untoward symptoms after inhalation. Irritation and dryness of the throat occurred very much less often in the second group; longer periods of relief were noted, and expectoration was facilitated. The solutions with added glycerin were as stable as were the unmodified solutions. Nine patients also used the modified solutions by continuous inhalation from a pressure tank apparatus and the majority received complete relief. Continuous inhalation by means of the above apparatus requires much less effort by the patient and the continued treatment is more effective.

Effect of aminophylline per rectum.—A preliminary report on the use of aminophylline rectal suppositories in the treatment of bronchial asthma is published by Dees². The suppository used consisted of 0.25 gramme of aminophylline in cocoa-butter with 5 or 7 per cent of wax. Clinical tests were made in 55 cases of severe bronchial asthma of mixed types. Many of the patients had acquired tolerance to oral aminophylline or to ephedrine. After the administration of aminophylline suppositories symptoms generally disappeared in 20 minutes and relief lasted for from 4 to 24 hours, even in status asthmaticus. In most cases the giving of 2 suppositories in 24 hours is sufficient to keep the patient symptom-free.

Evaluation of treatment methods.—An investigation has been undertaken by Westcott and Gillson to determine the clinical and physiological value of various methods of treating dyspnoea and anoxia due to chronic bronchial asthma. The results of inhalation therapy were observed and studies were made of vital capacity in a group of patients who had previously been treated by the usually accepted methods and who had undergone comprehensive physical examination. All the patients were given simple breathing exercises to increase the vital capacity of the lungs, and it was seen that simple mechanical exercises could be performed without difficulty and with some resultant increase in vital capacity by all ambulatory patients and by some bedridden patients with bronchial asthma. Postural drainage was of assistance in diminishing the amount of micropurulent respiratory secretions in cases of chronic bronchitis and also of bronchial asthma. Inhalation therapy with 1 in 100 adrenaline solution, used in conjunction with breathing exercises and with postural drainage, caused a substantial increase in vital capacity and a correspondingly greater relief from symptoms. In acute asthmatic states of mild or moderate severity inhalation treatment with 1 in 100 adrenaline hydrochloride conferred symptomatic relief equal in degree to that resulting from injections of 1 in 1,000 adrenaline hydrochloride in relatively larger doses, and with less systemic discomfort. No patients became adrenaline-fast after the above treatment, and hypodermic injections of adrenaline were still effective after continuous use of inhalation therapy.

Dees, Susan C. (1943)¹ *J. Allergy*, **14**, 469.

— (1943)² *ibid.*, **14**, 492.

Hurst, A. (1943) *Brit. med. J.*, **1**, 403.

Lockey, S. D. (1943) *J. Allergy*, **14**, 382.

Petersen, W. F., and Vaughan, W. T. (1944) *J. Allergy*, **15**, 97.

Rackemann, F. M. (1944) *New Engl. J. Med.*, **230**, 284.

Rogerson, C. H. (1943) *Brit. med. J.*, **1**, 406.

Tocker, A. M., and Davidson, A. G. (1944) *J. Allergy*, **15**, 108.

Westcott, F. H., and Gillson, R. E. (1943) *J. Allergy*, **14**, 420.

AVIATION MEDICINE

See also B.E.M.P., Vol. II, p. 239; Interim Supplement, No. 14*; and Cumulative Supplement, Key No. 116.

Physiology of aviation

Effects of flying on aviators

Visual problems.—The rapid advances of aeronautics have greatly increased the stresses to which aviators are subjected and long-distance night operations make night-vision and the effects of fatigue and boredom of great importance. Several factors in vision of especial significance in aviation are discussed by Weaver. These include the integration of sensation, perception and projection of light, colour vision, binocular single vision, accommodation and the mental aspect of vision. The factors peculiar to aviation which influence vision are anoxia, decreased barometric pressures, temperature changes, acceleration fatigue, nutrition, physical fitness and certain drugs. Visual acuity, colour vision and the size of the peripheral fields appear to be inversely related to the degree of anoxia sustained but probably represent only a small part of the total picture of anoxia. The effects of anoxia upon adjustive mechanisms, fixation, convergence and accommodation may be dangerous also. Changes in barometric pressure seem to have little direct effect on the eyes but cerebral ischaemia in blacking-out may affect the retinal arteries. Cerebro-retinal fatigue during long missions is combated by the use of special goggles but accommodative fatigue or spasm may be an additional hazard. Vitamin A, riboflavin and vitamin C are important in the nutrition of aviators, especially vitamin A in connexion with dark-adaptation. High blood concentrations of alcohol may cause disintegration of fusion of vision but otherwise the effects of alcohol are mainly on the central nervous system. Amphetamine (benzedrine) sulphate, pervitin and related drugs help to relieve boredom on long missions and Axis pilots are believed to use them. The effects of quinine and atebirin (mepacrine hydrochloride) on the eye have not been very significant but paroxysmal arterial spasm from their use has been reported by some workers. Carbon monoxide poisoning in aircraft is receiving considerable attention but up to the present time there do not appear to be any specific findings.

Diseases associated with aviation

Acute otitic barotrauma

Dickson, McGibbon and Campbell discuss the features of acute otitic barotrauma. Pain, deafness, injection and invagination of the tympanic membrane, effusion or bleeding into the middle-ear cavity and sometimes even rupture of the drumhead are due to the failure to adjust between atmospheric and intratympanic pressures. Permanent and temporary changes in the Eustachian tubes and fortuitous factors which interfere with auto-inflation are contributory causes. All degrees of the syndrome may occur and it was found that one out of every 5 members of air crews who were referred was suffering from this disability. Prophylaxis consists of prevention of the airman from flying while he is suffering from any upper respiratory infection, together with the use of self-inflation of the ears by Valsalva's method. Treatment should be instituted as quickly as possible; Valsalva's method, inflation by Politzer's bag and decompression in a suitable chamber are the principal available methods. In the consideration of the mechanics of the syndrome it must be noted that the proximal membrano-cartilagenous portion of the middle-ear cleft acts like a valve whereas the distal rigid-walled middle-ear cavities, consisting of the osseous tube, tympanum, mastoid antrum and air cells, are the parts affected by the vital changes. The walls of the proximal membrano-cartilagenous tube are in contact between the two open extremities—the nasopharyngeal ostium and the attachment to the margin of the osseous tube. In rapid descent, there is a time-lag factor in the opening of this area which prevents the escape of air down the tube and rapidly neutralizes the rarefaction of the air in the cleft. In this manner a primary pressure occlusion of the tube is produced. If the tube is not opened physiologically and air is not admitted to the middle ear, the occlusion becomes firmer as the descent on compression progresses until finally the occlusive force becomes greater than that which can be exerted by the muscles which normally open the tube. The hydrostatic pressure in the blood vessels which supply the middle ear is the sum of the existing atmospheric pressure plus the present blood pressure. Over-distension of the vessels by inequalities of pressure results in oedema, haemorrhage and effusion. These vital changes are confined to the middle ear and do not affect the compressible portion of the tube. Resolution begins when the amount of oedema and effusion is great enough to bring about equilibrium between the atmospheric and intra-tympanic pressures. The pathology of otitic barotrauma was experimentally studied in 18 cats. The changes were vascular in nature. Oedema, effusion, neutrophil polymorph emigration and haemorrhages were seen.

Air-sickness

Is it a neurosis?—Green considers the nature, prophylaxis and treatment of air-sickness. To nausea, vomiting, pallor and sweating are often added anorexia, dizziness and general nervous discomfort. Motion sickness does not explain air-sickness which occurs regardless of manoeuvring and despite position in the plane near the centre of gravity. Although generally related inversely to air-sickness experience does not guarantee immunity, but the relative immunity of pilots illustrates the advantage of experience and of occupation. Pilots in control are more immune than when they are flying as passengers, and radio-gunners, who are in the most confined space, are most affected. Of 1,106 individuals one half the number had experienced at least one attack during their flying career. Indisposition or over-night excess may cause transitory difficulties, but chronic air-sickness was found to be correlated to a neurotic trend of disposition. Aerobatics and flights during air turbulence involve exaggerated motion

of the airplane but involve also fear which appears to be the true source of the emotional conflict which fosters air-sickness. Air-sickness is aeroneurosis. The incidence of air-sickness in Green's series coincided remarkably with the accident rate. Prophylaxis entailed gradual adaptation to air conditions by means of initial short flights and simple missions. Treatment, based on the supposition of aeroneurosis, consisted of encouraging explanations before graded flights were undertaken starting with 20 minutes in a reputedly safe aircraft. Before taking off, each individual received orally 0.1 gramme of pentobarbital sodium (nembutal) and 0.0013 gramme of atropine sulphate. When 3-hour flights were accomplished without distress transfer was made to a combat plane and medication was gradually withdrawn. Of 35 men so treated 10 were cured; 9 returned, improved, to probationary status in crews.

Effects of anoxia

Tests for prospective pilots.—Aviation medicine is primarily concerned with problems arising from anoxia. Groesbeck describes the application of the low-pressure chamber to the elimination of the physically inadequate and the instruction of the accepted recruit in the use of oxygen apparatus. Two standardized 'runs' in the low-pressure chamber are substituted for flights at certain ranges of altitude. In the demonstration of the effects of anoxia complicated psychological tests have been replaced by a simpler test of crossing out letters in a jumbled alphabet. Lately a self-recording contrast test, dependent upon the loss of visual discrimination, has come into use whereby the student can picture vividly the errors of his performance. In the first run the student is taken to a simulated altitude of 18,000 feet and remains there until conscious of the handicap imposed by anoxia in the performance of the tests. He then puts on an oxygen mask, is elevated to 28,000 feet and repeats the tests. The principles and importance of oxygen absorption are explained to him thoroughly. Rapid descent ensues, coordinated with the student's adaptation of ear pressure. Failure to adjust this pressure may result in painful, possibly serious, otitis media. An accurately fitting mask is essential whether administration is by rebreathing, demand or constant flow. The reactions of cyanosis, convulsions and unconsciousness do not exceed 8 per cent of instances; circulatory collapse is rare. In the second run the cadet as he reaches the equivalent of 35,000 and 40,000 feet is exposed to air embolism ('bends'). Bends include excruciating joint pain, respiratory difficulty denominated 'chokes', or—a more serious symptom—substernal pain of cardiac origin. Bends may develop at any time on actual flight from dietary indiscretion or insomnia but generally an individual who suffers from incapacitating bends during two consecutive runs is probably an unsuitable recruit. From the instructional standpoint the pupil acquires the indispensable knowledge that above 34,000 feet 100 per cent of oxygen is essential to him and, slight anoxia notwithstanding, is adequately protective.

Hyperventilation

Symptoms and treatment.—The syndrome of hyperventilation with tetany is reported by Carryer. Hyperventilation occurs often in the Forces and is as often missed. It is a risk to aviators. Anxiety, fear or fatigue bring it on in nervous people, but stable persons such as pilots in the Air Force, when in danger, may also develop it. There are two forms: in one the breaths taken are consecutive and rapid, and in the other there is a deep sighing. Hyperventilation results from stimuli in the cerebral cortex which affect the respiratory centre. Another type may originate from the hypothalamus or again from the lower centres. It may also develop as a result of oxygen want. Symptoms appear because alkalosis develops. There is lightheadedness, tingling of the fingers and toes, and a sense of suffocation; as the symptoms progress, panic develops. Effort syndrome is said to be produced by hyperventilation. The treatment is carried out by giving mild sedatives, calcium salts and acid residue diet.

Pneumothorax

Tests with regard to air transport.—The possibilities of air transport for wounded persons and of making use of pilots who have undergone pneumothorax treatment has prompted Todd and Anderson to examine the effects of altitude in cases of pneumothorax with the object of finding the optimum flying height and the adjustments which may be necessary before or during flight. Four individuals with pneumothorax and one with broncho-pleural fistula in addition, were used for the tests; in 3, including the last, the condition was right-sided, in 2 left-sided; in one of each type the mediastinum was fixed. Each was placed in a pressure chamber and 'taken up' at a rate of 500 feet a minute. Tests of the vital capacity and alveolar air, electrocardiograms and X-rays were taken at 2,000, 4,000, 6,000 and 8,000 feet and afterwards at each 1,000 feet until the maximum height considered to be safe for each patient had been reached. The conclusions drawn were that it is dangerous to transport by air persons suffering from tension pneumothorax at any height without putting a needle in the chest, to be left in position during the whole flight. For cases of chest wound the level of the flight should not exceed 4,000 feet and for pilots the safe maximum is 6,000 feet. Even the patient with a broncho-pleural fistula experienced dyspnoea and pain at about 6,000 feet. The symptoms are caused by expansion of the air in the pneumothorax cavity with consequent rise of pressure. Fixity of the mediastinum aggravates the effects of altitude.

Carryer, H. M. (1943) *Proc. Mayo Clin.*, 18, 522.

Dickson, E. D. D., McGibbon, J. E. G., and Campbell, A. C. P. (1943)

J. Laryng., 58, 465.

Green, D. M. (1943) *J. Aviat. Med.*, 14, 366.

- Groesbeck, B. (1944) *Ann. intern. Med.*, **20**, 367.
 Todd, G. S., and Anderson, D. M. (1943) *Lancet*, **2**, 597.
 Weaver, E. M. F. (1943) *J. Aviat. Med.*, **14**, 289.

BACKACHE AND LUMBAGO

See also B.E.M.P., Vol. II, p. 251; and Cumulative Supplement, Key No. 117.

Abnormalities

Sacralization of the 5th lumbar vertebra

Clinical picture and treatment.—Zadikoff describes a backache of 2 years' duration arising from incorporation of the fifth lumbar vertebra in the sacrum with consequent nipping of the soft tissues between the ribs and the iliac crest. The pain which occurred suddenly in 1941 while the man was bending was severe, leading to vomiting and to the suspicion of renal colic for which morphine was given. This pain became localized to a parallelogram situated between the last palpable rib and the iliac crest and limited anteroposteriorly by lines drawn from the axillary folds. The patient, a corporal of the Royal Air Force, continued on duty although in constant pain until 1943, when he noticed mucus in the stools. Examination showed disappearance of the lumbar curve and diminished lateral flexion of the spine. The urine was normal in composition and voidance and nephroptosis was excluded by pyelogram. Radiography portrayed the abnormality of the lumbar vertebrae and excluded the presence of a lumbar rib pressing on the right kidney. Injection of novocain (procaine hydrochloride) into the twelfth dorsal nerve gave 3 hours' relief. Owing to the shortness of the twelfth rib the eleventh was held responsible and was resected. Complete relief followed, the lumbar curve returned, lateral flexion of the spine increased and mucus disappeared from the stools. The unilateral distribution of this type of backache remains unexplained.

Postural defects

Classification of lesions

'*Shop-girl's hip*'.—Burt discusses the prevention and treatment of low-back pain. The pathology of many conditions which give rise to low backache is obscure. The author considers two main groups of cases, namely those due to faulty posture and those with lesions in the deep structures of the back and buttocks. To the latter group Steindler has given the name, posterior division syndrome; such cases include those previously classed as lumbo-sacral and sacro-iliac strain. Both types in the main groups are common and both can be treated satisfactorily by physical methods. Faulty posture may be a primary cause of backache or it may predispose to persistent pain as a result of acute or chronic strain; in any case recovery is delayed when there is also an associated postural defect. Four main types of postural abnormality are recognized, namely lordosis, flat back, sway back, and the syndrome of the 'shop-girl's hip'. Postural backache occurs after long hours of work and is relieved by rest. In chronic lordosis shortening occurs in the erector spinae muscles and also in the fascial tissue so that elasticity of the parts is reduced and the muscles are constantly in spasm. Most cases of postural backache could be prevented by early treatment of postural faults. Cases which date from pregnancy are common but could be prevented by exercise started in the early part of the puerperium. Examination of the back should be a routine part of the second postnatal examination. Suitable exercises are described and may be used in conjunction with heat and massage if required. Six common sites for localized pain which produces lesions in the back have been described by Steindler who considers that trauma may be responsible in many cases. The diagnosis is made by novocain (procaine hydrochloride) injection tests the technique of which is described. The most common site for such lesions is in the lumbo-sacral region. The ilio-tibial band is also the site of pain in many cases and lesions may co-exist in both regions. The problem of treatment is made more complex by the difficulty of accurate diagnosis and by the fact that cases are often of long standing before advice is sought. In many postural cases and in early cases of the posterior division syndrome physiotherapy and novocain injections give good results but in chronic cases of the latter type in-patient treatment may be required for manipulation and subsequent physiotherapy; if these fail surgical methods must be instituted. The possible development of a functional element in chronic cases must not be overlooked.

Burt, H. (1944) *Brit. J. phys. Med. N.S.*, **7**, 11.

Zadikoff, I. J. (1943) *S. Afr. med. J.*, **17**, 299.

BARTONELLOSIS

See also B.E.M.P., Vol. II, p. 296; and Cumulative Supplement, Key Nos. 121 and 122.

Oroya fever (generalized bartonellosis)

Immunology

Statistics of cases examined.—An immunological study of Carrión's disease has recently been carried out by Howe^a in the regions near Lima, Peru, in which it is endemic. The disease is caused by infection with *Bartonella bacilliformis* carried by the wild sand-fly (*Phlebotomus noguchi*). The fly bites only at night, and complete protection can be assured only by quitting before nightfall the rather narrow strip of country between 800 and 3,000 metres above sea-level where phlebotomus occurs. A total of 203 persons was examined. (1) Sixteen of them

had clinical signs of bartopellosis and positive blood cultures; all showed a significant rise in serum agglutinin titre during the course of their illness. (2) Nine patients with typical verruga peruana (the later stage of Carrión's disease) and positive blood cultures showed a higher average titre than those of the former group. (3) Six with similar clinical signs but negative blood cultures had high titres. (4) Fifteen patients had a typical eruption and positive blood cultures but their serums did not show any agglutination. (5) Of 9 individuals without symptoms, 8 of whom had positive blood cultures, one only showed agglutination. A history of past infection was given by 3. (6) Six patients who had neither signs nor history of bartonellosis and negative blood cultures gave positive agglutination tests. Thus a considerable number of carriers were discovered. Such persons may represent a natural reservoir of infection.

Treatment

Immune rabbit serum.—A specific treatment has not yet been established for Oroya fever, the severe and often fatal anaemic stage of Carrión's disease. Howe¹ however, of the Department of Comparative Pathology and Tropical Medicine, working in conjunction with Franco of the National Institute of Hygiene and Public Health, Lima, Peru, has reported in detail 3 cases of severe Oroya fever in none of which was there any dramatic event as a result of the administration of hyperimmune rabbit serum with a high titre of agglutinins for *Bartonella bacilli*. Immune serum of high agglutinin was produced in rabbits by the intravenous administration of large amounts of *Bartonella bacilliformis*.

Howe, C. (1943)¹ *Arch. intern. Med.*, **72**, 147.

— (1943)² *ibid.*, **72**, 429.

BED-SORES

See also B.E.M.P., Vol. II, p. 302; and Cumulative Supplement, Key No. 123.

Aetiology

Influence of hypoproteinaemia

Mulholland, Tui, Wright, Vinci and Shafiroff have investigated 35 unselected cases of bed-sores (decubitus ulcers) in order to study the part played by hypoproteinaemia in their formation. All the patients were in a poor nutritional state, and none had a plasma protein concentration above 6.35 grammes per cent. The number and extent of the ulcers appeared to be related to the plasma protein deficiency. Two of these patients were placed on a high protein diet and rapid healing of the bed-sores ensued. In 8 other hospital ward patients with bed-sores there was a negative nitrogen balance and loss of weight, although 2 of them were given a higher caloric diet than the normal. When each of these 8 patients was given a high protein diet (by the addition of an amino-acid dextrose mixture), the nitrogen balance became positive and signs of healing in the ulcers became apparent in about 4 days. The experimental omission of fatty acids indicated that they are not essential to induce healing in bed-sores. The small changes in the haematocrit readings made during the period of observation suggested that anaemia was not a predisposing factor in the formation of the ulcers. Vitamin therapy, which was given throughout each patient's stay in hospital, did not prevent their formation when hypoproteinaemia coexisted. It seemed evident that at certain levels of malnutrition associated with protein deficiencies the effect of pressure on the recumbent body induced local tissue necrosis.

Mulholland, J. H., Tui, Co, Wright, A. M., Vinci, V., and Shafiroff, B. (1943)
Ann. Surg., **118**, 1015.

BLADDER DISEASES

See also B.E.M.P., Vol. II, p. 374; and Cumulative Supplement, Key Nos. 136-146.

Neoplasms

Malignant growths

Ureteral transplantation.—In order to eliminate cases unsuited to his method of two-stage uretero-sigmoidal implantation with cystectomy, Jewett classifies vesical tumours into 3 groups. (1) Non-infiltrating tumours the diagnosis of which is established cystoscopically. Fulguration or loop resection succeeded by the use of radium is appropriate treatment. (2) Infiltrating tumours confined to the bladder wall. Bimanual examination under anaesthesia to establish mobility should be used and, if necessary, deep biopsy to supplement cystoscopy. Only cases showing free mobility offer hope of radical cure by this operation. (3) Tumours showing circumvesical extension palpable to bimanual examination and often with metastases. A hopeless prognosis forbids two laparotomies, but the existence of pain and haemorrhage, uncontrollable otherwise, may compel a one-stage transplantation and cystectomy later if the diversion of urine affords insufficient relief. The first stage of the operation leaves 5 centimetres of each intact ureter imbedded in the anterior longitudinal muscular band of the sigmoid. The sigmoid is approximated to the ureters, and rotated to bring the anterior longitudinal muscular band into apposition, so that the part adjacent to each ureter serves for the imbedding. The sigmoid requires to be anchored to the posterior peritoneum. A month later the ureter is severed 3 centimetres below its emergence from its sigmoid bed. The distal end is ligatured, and through the proximal end the specially designed

electrode is pushed 1.5 centimetres upwards. This electrode is insulated throughout, save for a minute aperture 1 centimetre from its end for extrusion of a cutting wire manipulated by a lever, pressure on which cuts the widely patent ostium. Operative success was attained in 26 out of 29 cases.

Indications for ureteral reimplantation.—The main indication for reimplantation of the ureter into the bladder, state Stevens and Marshall, arises with partial cystectomy for neoplasms involving a ureteric orifice. Injury during operation, labour or otherwise is a second indication. Thirdly, intrinsic or extrinsic obstruction of the lower part of the ureter, its extravascular opening, or ureterocele, may demand this procedure. Adequate renal parenchyma and length of ureter are essential. Severe infection of bladder or ureter forbids the operation. All authorities insist that the operation must be extraperitoneal and devoid of tension and that the bladder must be kept at rest by suprapubic or urethral drainage. The authors, detailing their procedure, prefer oblique insertion into the bladder of the ureter, one centimetre of the vesical end of which is bisected to produce a 'fish-mouth'; the lips of this are sutured to mucosa and submucosa by intravesical stitches only. Objection to intravesical stitches is unfounded. Direct insertion, a single incision producing an elliptical termination to the ureter and stitches extravascular, intravesical or both, are modifications elsewhere advocated. Of 10 patients thus treated, 9 had vesical carcinoma and the tenth had fibrous obstruction. Observations on 9 patients who survived operation showed that ureters pre-operatively dilated remained enlarged, but that dilatation had not arisen from operation. Renal function had not deteriorated but had improved. Late post-operative cystograms obtainable in 4 cases only showed one instance of slight reflux after 8 months, one of pronounced reflux within a few weeks, and in 2 cases complete absence of ureteral reflux.

Results of interstitial radiation.—From 400 cases of vesical tumour seen during 9 years Jacobs selected 93 as appropriate for radium treatment. The ulcerous, the nodular and especially the broad-based papillary carcinomas occupying the basal zone constituted the majority of the tumours. Subjects were selected mainly by cystoscopic examination and all possible knowledge was gathered from pyelography, urinary estimates and cystograms. Radiography of the chest and of the upper part of the femur gave evidence on the presence or absence of metastases. Diathermic removal of the growth down to the mucosa was effected through a suprapubic extraperitoneal cystotomy. Then needles containing 1.0 and 0.5 milligramme of radium were so disposed as to afford homogeneous irradiation to the tumour base. The dosage was approximately 7000 r and, varying with the extent of the lesion, the needles remained in situ for from 120 to 200 hours. Eight patients succumbed within a month of operation and necropsy emphasized ascending infection as the outstanding danger. Twenty-six died later of the disease, 15 within one year, 8 within 2 years. Two outlived 3 years and one, in whom alone the cystoscope showed a period of freedom from growth, outlived 6 years. In the last 11 patients survival exceeding a year, with relief from haemorrhage and pain, certainly vindicated operation. There is also a group consisting of 11 patients alive but with their disease, of from one to 5 years' standing, uncontrolled. Three patients were untraced and 4 had died of intercurrent causes after an average of 4 years' immunity. Forty-one are alive and well, of whom 31 are shown cystoscopically to be tumour-free, 10 having enjoyed from 4 to 9 years of immunity. The others were unavailable for examination.

Treatment by X-ray therapy.—Colby and Schulz review the results of treatment with super-voltage X-rays over a 5-year period in 139 cases of malignant neoplasm of the bladder. The average age was 61 years and about two-thirds of the number of patients were males. The average delay from the time of the first significant symptom to admission for treatment was 15.7 months. The authors insist that operation is the best method of treatment but in none of the cases was such procedure possible on account of the general condition, extent of the growth or the patient's refusal. The conclusion formed from a study of biopsies was that the most undifferentiated types responded best. Approximately one-third of the number of tumours disappeared or were reduced to a small fraction of the former size. Symptoms were relieved in over half the number of treated cases. There was not any difference in the response of the papillary and non-papillary neoplasms. The best results were obtained in cases in which, as a result of external irradiation, other agents such as radium and high-frequency current could be employed. According to these investigators there appears to be justification for the use of external radiation for patients with advanced cancer of the bladder.

Stone

Aetiology

Urinary lithiasis in children.—Smith reviews the features of urinary lithiasis in childhood. A survey of the literature of European countries and of the United States of America during recent years indicates that lithiasis in childhood does occur, although infrequently. Between 60 and 70 per cent of the calculi are found in the lower urinary tract (bladder and urethra) and multiple calculi are commoner in children than they are in adults. All ages under adolescence are affected and stones have been reported in the foetus; the age of onset is usually difficult to determine since the calculi are often of large size when first diagnosed. In the aetiology of lithiasis there is a difference of opinion regarding the importance of the precipitation of uric acid crystals in the kidney during the first months of life. American authors have stressed the frequency with which stone and congenital abnormalities co-exist.

Anomalies of the urinary tract are not rarities and various post-mortem studies show an incidence of from 2 to 13 per cent of deviations from normal conditions. Divergent views have been expressed on the primary or secondary origin of stricture and of dilations, whether congenital and complicated by stone or actually resulting from the latter. Whereas a large number of observers have found calculus formation to be associated with demonstrable abnormalities, stones are just as often found without such anomalies. Summing up this aspect of urinary lithiasis, Smith concludes that one should bear in mind the possibility of congenital malformations in encountering a calculus in a child. The symptomatology does not appear to differ from that in later life; pain, haematuria, urinary frequency, painful micturition, occasional enuresis, the passage of a stone, possible signs of infection and sometimes gastro-intestinal attacks are the symptoms recorded. Available reports are too few or are supported by too short observation to establish facts upon which prognosis may be based. On the whole there is a conservative outlook in the treatment of renal and ureteral stones; urethral stones seldom require treatment unless obstruction is present. The author stresses the importance of the recognition of any congenital anomalies which may be present with the calculus as their presence or absence must be a decisive factor in the choice of treatment.

Nervous diseases

Incontinence

Aetiology in the female.—Sure enumerates the causes of urinary incontinence in the female and describes his procedure in certain conditions. Over-distention of the bladder in puerperal or post-operative periods may be diagnosed by the presence of a large amount of residual urine in the bladder after it has been emptied by catheter; one ounce of $\frac{1}{2}$ per cent mercuriochrome solution deposited in the bladder is a prophylactic procedure. If required, an indwelling catheter, preferably Foley's, is satisfactory. In senile atrophy of the bladder and urethra, ovarian inactivity is indicated by a vaginal smear the staining reaction of which to the lugol fume method of Mack shows an absence of glycogen. Such cases yield to oestrogenic medication. Urethral strictures yield to dilatation with Hegar's cervical dilators. In non-senile atrophy voluntary contractions and relaxations of the sphincter over a Hegar's dilator are practised, alternately checking and permitting the urinary stream. Repetition of the procedure every 2 hours leads to recovery of control. Cystocle which causes urinary incontinence is best remedied by the Manchester operation. Surgical removal is necessary for tumours of the cervix and of the anterior triangle. When urinary incontinence arises from retroversion of the uterus which brings the cervix under the neck of the bladder the conditions are best remedied by the Gillian form of suspension. When traction of adhesions to the pubic rami or lateral connective tissue maintains a patent urethra, the latter must be freed from adhesions and supported from below. Employment of the bulbo-spongiosus muscle and fat according to the method of Martius has proved to be satisfactory. It is mentioned that for a uretero-vaginal fistula which does not heal within a month nephrectomy is preferable to plastic operation.

Extroversion

Treatment

Operative procedures.—Ectopia vesicae if it is left untreated causes death from renal complications in 66 per cent of cases before the sufferer reaches his twentieth year. Higgins advocates operation within the first 6 months of life rather than at the fourth or fifth year. The correction of epispadias however should be delayed until the child is 5 or 6 years old. Early operation for ectopia vesicae forestalls infections of the urinary system and dilatation of the ureters from uretero-cystic obstruction. In Higgins's cases for 5 days before operation a saline enema and 6 doses (totalling 0.25 gramme per kilogram of body weight) of sulphasuxidine (succinylsulphathiazole) were administered daily. On the day before operation only glucose and water were ingested. Enemas were administered until the return was clear of faecal content; paregoric $\frac{1}{4}$ – $\frac{1}{2}$ drachm, according to age, was given thrice daily. An injection of atropine was given before operation. Under anaesthesia the right ureter was transplanted into the rectosigmoid at the first operation; the left ureter was transplanted 10 days later and the ectopic bladder was removed. A modified Coffey technique was employed, the narrow lumen of the ureter and the thin muscularis layer of the infantile rectosigmoid requiring extreme delicacy of procedure. A rectal tube was inserted at the operation to remain in place for from 7 to 10 days; frequent irrigations maintained potency. Paregoric was continued during the first day after operation and for 2 days a lateral decubitus was maintained in order to prevent aspiration of vomited matter. Oral intake was supplemented by subcutaneous infusion and, when necessary, blood transfusion. In the series of 19 cases one infant died of broncho-pneumonia and one from aspiration of vomited matter. The remaining 17 left hospital in good condition and are making satisfactory progress.

Ureteral transplantation: a survey.—Turner describes the later condition of patients subjected to ureteric transplantation. Of 17 original patients 4 succumbed to operation; 2 died subsequently after supplemental operations and one from intestinal obstruction. Nine survive and hold their place in life without any evident renal deterioration. Between 4 and 6 years of age is the favoured age for operation but health is the criterion and this must be brought to its best, especially with regard to renal function. It is essential to plant the ureter obliquely into a submucous bed in the bowel, avoiding kinking, and with due regard to the

ureter's blood supply. Implantation of both ureters into the mesial side of the bowel is recommended, picking up the left ureter external to the sigmoid and bringing it through the mesocolon to enter the bowel 1½ inches above its fellow. Preservation of the alignment occupied in its retroperitoneal bed brings the right ureter into the lowest part of the sigmoid or uppermost part of the rectum. Simultaneous implantation of both ureters grows in favour as a procedure, perhaps even for children, otherwise 3 weeks is a proper interval to allow between the transplantations, providing all goes well. The urine is stored in the large bowel, not in the rectum, and control is quickly acquired. The scope of the procedure widens from its first application in children to ectopia vesicae and its congener complete epispadias, or in the female subsymphysial epispadias. It now applies to adult ectopia vesicae, to cystectomy for neoplasm, to certain cases of cancer of the cervix and to intractable vesico-vaginal fistula. It may occasionally solve problems in the systolic bladder after a successful nephrectomy for tuberculous kidney, and in severe urethral injuries.

Colby, F. H., and Schulz, M. D. (1943) *Radiology*, **41**, 371.

Higgins, C. C. (1943) *J. Urol.*, **50**, 657.

Jacobs, A. (1943) *Brit. J. Urol.*, **15**, 79.

Jewett, H. J. (1943) *Brit. J. Urol.*, **15**, 121.

Smith, C. C. W. (1944) *Acta chir. scand.*, **90**, 1.

Stevens, A. R., and Marshall, V. F. (1943) *Surg. Gynec. Obstet.*, **77**, 585.

Sure, J. H. (1943) *Urol. cutan. Rev.*, **47**, 399.

Turner, G. G. (1943) *Brit. med. J.*, **2**, 535.

BLASTOMYCOSIS

See also B.E.M.P., Vol. II, p. 403.

Blastomycetic dermatitis

Treatment

Effect of sulphonamides.—Infection with blastomycosis, an affection which is due to a yeast-like organism, has been known in man since 1894. It is a rare disease with two main forms, cutaneous and systemic. Albert describes a patient aged 50 years, with cutaneous lesions on the site of an old keloidal scar on the left foot, and other lesions also on the left leg, right groin and left elbow. The largest was an ulcerated area 7 inches by 9 inches in extent on the outer side of the left thigh consisting of raw violet-red granulation tissue. The margin, which was half an inch wide, was seriginous and heaped up, with many small skin abscesses. Scrapings showed a yeast-like organism which was identified as *Blastomyces hominis*. There was not any evidence of systemic spread. Intensive potassium iodide therapy did not help. A dressing of 12½ per cent sodium sulphate was applied and sulphonamides were given intensively. Eighty grammes of sulphapyridine were given in 16 days; after 14 days' rest, 70 grammes of sulphathiazole were given in 16 days, and after a further rest of 14 days 36 grammes of sulphathiazole were given in 8 days. The only complication was a slight haematuria which occurred after the second course of treatment, by which time most of the lesions had disappeared. During the periods of rest from the taking of sulphonamides, there was not any evidence of healing. Acute lobar pneumonia developed later from which the patient recovered after 22 grammes of sulphapyridine had been administered in 4 days.

Albert, M. (1943) *Brit. J. Derm.*, **55**, 294.

BLINDNESS

See also B.E.M.P., Vol. II, p. 407; and Cumulative Supplement, Key Nos. 149–162.

Congenital defects

Choroid, retina and iris

Hemeralopia: dark-adaptation tests.—Michaelson describes the results of dark-adaptation tests performed on a series of soldiers complaining of defective night vision. Koch's dark adaptometer was used. The minimum light sense and form sense were tested in some cases after 3 minutes and in all cases after 30 minutes. The reliability of the instrument was tested by measuring the light sense minimum in the same individuals on several occasions. A series of normal individuals were first investigated for the purpose of determining the average light sense and form sense minimum after 3 minutes and 30 minutes respectively. The data provided by the measurement of the minimum form sense, which was taken by using the rotating E, were found to have a wide range, and suggest that the deviation probably depended upon other factors.

The minimum light sense after 30 minutes in all cases of organic ocular disease was significantly raised. The remainder of the patients complaining of defective night vision, who all had proved neurosis, had an average minimum light sense which was only slightly above the normal and some of them showed abnormal day to day variations. In both groups of cases, the minimum form sense was raised.

The writer's conclusions are that the minimum form sense and light sense together, measured after 30 minutes, constitute a sufficient criterion of the individual's ability to see in the dark. In all cases of defective night vision patients have a poor minimum form sense. The association of a good light sense minimum with poor minimum form sense is suggestive of functional

disturbance as the cause of the defective night vision. Dark adaptometers which measure the minimum form sense and not the minimum light sense have a limited usefulness on account of the great variation in the minimum form sense even among subjects not suffering from night blindness.

Trauma

Perforating wounds

Removal of foreign bodies.—Stieren emphasizes that prompt and proper methods in dealing with intra-ocular foreign bodies will save many injured eyes and will enable a certain amount of vision to be retained. If the foreign body should be non-magnetic the treatment will be more difficult. A dose of 1,500 units of tetanus antitoxin should be given in every case, not only because of its specific action but also because it is a foreign protein which encourages antibody production. Then the wound of entrance should be accurately located and the position of the foreign body determined. Ophthalmoscopy will often disclose the position but localization by means of X-ray examination may be necessary. With the exception of glass all foreign bodies act as continuous irritants; brass and copper are particularly toxic and retention of steel and iron is followed by a deposit of iron throughout the eye-ball (siderosis bulbi). Stieren prefers general pentothal anaesthesia for removal of foreign bodies from the iris because of the danger that the body may be squeezed through into the vitreous by the patient's movements. If the lens contains a foreign body, lens extraction should be carried out at once. Prolapsed iris through a corneal wound should be excised and the latter sutured. If the wound of entrance involves the ciliary body Stieren enucleates the eye, considering it better to lose one eye than to risk the possibility of sympathetic ophthalmia. He emphasizes the dangers associated with the use of the giant magnet since its use may inflict more damage on the eye than did the original injury. He has never found the hand magnet to fail him. He removes a magnetic foreign body through the cornea when it is anterior to the posterior lens capsule and through a scleral incision when it is in the vitreous, in the choroid or in the optic disk. Stieren considers the fear that retinal detachment will result from transcleral extraction to be exaggerated. His scleral incision is made down to the choroid and does not penetrate the vitreous; an important point is that before the conjunctival flap is sutured into place, the scleral incision is touched with pure phenol. This induces a choroiditis locally and prevents retinal detachment. The author deplors the use of the magnet as a diagnostic instrument for the purpose of determining whether or not ferrous metal is within the globe. In the prevention of subsequent inflammations of the uveal tract Stieren has found the use of sulphonamides to be disappointing and he employs infections induced by the giving of injections of foreign protein or typhoid vaccine. When a purulent infection of the cornea ensues the eye-ball is enucleated.

Tumours

Tumours of the orbit and its walls

Prosthetic restoration of orbital contents.—The innumerable facial mutilations which are inevitably to be found among war injuries present problems not only of aesthetic results but also of surgical shortage and of financial limitations. In considering facial reconstruction Gerrie states that tediously repeated operations must yield to speedier prosthetic restorations. Materials hitherto employed such as wax, paraffin, celluloid, gelatin, vulcanite, aluminium and gold lack durability or verisimilitude. Vulcanite, when concealed, served well but now polymerized resins supersede it as they are translucent and comfortable; they are however difficult to tint to an acceptable skin colour. Raw latex rubber, introduced into the field of plastic surgery by Bulbulian, is life-like; even flexible fingers based on wire cribbing have been formed of it, but the fact that it shrinks and that its colour fades are disadvantages. The reconstruction with latex rubber of an orbit disfigured by operation for sarcoma is described by Gerrie. As a copy, a mask of the face showing the sound orbit was obtained and a separate two-sectional model of the deformed orbit was made, the impression material used, negocoll, giving accurate reproduction of the undercuts. The model was filled with dental wax in which the glass eye was embedded. The wax was then carved so as to duplicate the sound orbit. A window cut in the wax behind the glass eye allowed its removal and after adding a rim round the window for retention of the eye, the model was invested to complete the 'master-mould'. The rubber, tinted after many trials with varied proportions of vermilion, ochre and yellow pigment, was packed and self-vulcanized in the form left after the wax had been boiled out. The pressing of the eye into its chamber, the designing of an eyebrow and the adaptation of glasses already worn for astigmatism completed the prosthesis. Continual advance is being made in plastic productions and artificial eyes made of these materials are now replacing glass eyes the supply of which is restricted by war-time conditions. The vinylite resins are already being used and other materials are being subjected to experiment under the auspices of the National Research Council of Canada.

Gerrie, J. (1943) *Canad. med. Ass. J.*, **50**, 104.

Michaelson, I. C. (1944) *Brit. J. Ophthalm.*, **28**, 140.

Stieren, E. (1943) *J. Amer. med. Ass.*, **123**, 880.

BLOOD EXAMINATION

See also B.E.M.P., Vol. II, p. 457; and Cumulative Supplement, Key Nos. 163–169.

Cellular changes (blood count)

Value and significance of the indices and absolute determinations

Corrections for iron and oxygen.—Macfarlane and O'Brien discuss the difficulties met with in determining the mean oxygen capacity and iron content of blood of a colour equal to 100 per cent of the British Standards Institution colour standard. They found that the measurements obtained were not strictly in proportion to the readings obtained with the Haldane-Gowers haemoglobinometer and the spectrophotometer. The authors discuss possible causes for the variability; part was due to technical error and part to a sex difference which was observed in the relative proportions of the colour, iron, and oxygen capacity of haemoglobin. The authors consider that the National Physical Laboratory efficient comparator should be used for colour estimation of haemoglobin in future, as the Haldane-Gowers haemoglobinometer shows a large variability. King, Gilchrist and Matheson state that most of the medical records of haemoglobin concentrations are in terms of the Haldane standard. The authors have calibrated their tubes of Haldane standard by reference to bloods the haemoglobin content of which has been assessed by iron analyses and by comparisons with photometric haematin results. As a result of their measurements the authors have determined that the colour of the British Standards Institution Haldane standard is equal to that given by blood of 19.8 millilitre oxygen capacity (14.8 gramme haemoglobin) per 100 millilitres, and not of its stated strength of 18.5 millilitre of oxygen (13.8 gramme haemoglobin). The haemoglobin results of the Haldane method agreed with those reached by the alkaline haematin methods when the correction for the Haldane standard was applied.

Observations on the red cells in a stained blood film

Oval cells.—Penfold and Lipscomb describe a Jewish family with two rare abnormalities. The first is elliptocytosis (oval erythrocytes) an abnormality not previously reported in Great Britain although described in America and on the continent of Europe. The second anomaly is of the vascular system, namely hereditary haemorrhagic telangiectasis; this has been described in Great Britain and in this century by Osler and by Parkes Weber. The oval-celled trait has been called olliptycotosis, elliptocytosis, ellipsocytosis, ellipsocythaemia and 'cameloid blood'; instead of being circular bi-concave disks the cells are predominantly oval or elliptical in shape. Oval cells must not be confused with sickle-cells. McCarty among 10,000 routine blood examinations met with 4 cases only; the abnormality was first described in 1904 by Dresbach, it is now said to have been seen on from 350 to 400 occasions and according to Mendel's law it is of a dominant character.

Coagulation (blood platelets)

Platelet count

Wright investigated the sources of blood platelets and their adhesiveness in experimental thrombocytosis. Intravenous injections of pyridine in rabbits produce an increase in the number of platelets and in their stickiness. Adrenaline administered intravenously resulted in an increased number of platelets but not in alteration of the adhesiveness. Splenectomy resulted in a rise in the platelet count for 7–10 days and also in an increase in the stickiness. During this post-operative period pyridine produced a response which was least noticeable when the number and the stickiness of the platelets were maximal in response to the surgical trauma. As the platelet count returned to the normal the effect of pyridine again became pronounced. The giving of adrenaline did not have any effect on either the number or the adhesiveness of the platelets after splenectomy. The author suggests that adrenaline acts by producing a rapid outpouring of mature platelets from depots in the spleen whereas pyridine, like the stimulus of surgical trauma, increases the output of new platelets from the bone marrow.

Serological tests

Agglutination tests

The Rh factor.—In a report on the presence of the Rh constituent in the Indian population of Calcutta, Grevil and Roy Chowdhury recognize three degrees of agglutination: (1) strongly positive, with centrifugal clumps, (2) positive, with centripetal clumps only and (3) doubtful, with granulation which disappears when the fluid is agitated and reappears when it is again undisturbed. In negative agglutination the erythrocytes remain suspended. The erythrocytes of 200 individuals were obtained from the Red Cross blood bank and a second category consisted of the erythrocytes of husband and wife whose history was suggestive. Essays with the serums of mothers or erythroblastotic infants and other serums proved to be unsatisfactory, and the authors therefore publish only the results obtained with a successful anti-Rh rabbit serum. This serum, which was obtained by injecting the erythrocytes of *Macacus rhesus*, agglutinated in 1 hour—before and after inactivation—a 2 per cent suspension of the erythrocytes of *Macacus rhesus* in a dilution of 1 in 300. Investigations with dilutions of 1 in 10 and 1 in 25 of the inactivated serum showed the Rh constituent to prevail in 90 per cent of Calcutta Indians, in contrast to 85 per cent in white persons. The gradations of intensity of reaction from 43 strongly positive through 120 positive and 17 doubtful to 20 negative suggest a quantitative variation rather than the qualitative difference which demarcates the recognized blood groups. Successful readings after the use of a possibly iso-immune serum may determine the status of the Rh constituent as a new antigen.

The Rh factor and slide technique.—Simmons, Graydon, Jakobowicz and Bryce report the

incidence of the Rh factor in Red Cross blood donors in Victoria, Australia. Of over 3,600 blood samples tested with a special high titre human anti-Rh serum, using the slide technique, 17.7 per cent were Rh negative. None of the samples classified as Rh negative by this method reacted with a standard anti-Rh guinea-pig serum when tested by the standard tube method. Of 185 blood samples which were Rh negative when tested with the human anti-Rh serum 14 gave positive results when retested with 4 other recently acquired human anti-Rh serums when the slide technique was used and with the guinea-pig anti-Rh serum when the tube technique was used. The difference between the percentage of Rh negative subjects in blood group A and in other groups suggests that the Rh factor may not be entirely independent of the ABO system. The authors' work confirmed that the Rh factor is not a single entity and different human anti-Rh serums give results which although substantially in agreement show occasional discrepancies. Human anti-Rh serums selected for testing purposes should therefore be those which in combination detect the greatest percentage of Rh positive blood samples. The authors' control tests showed perfect agreement between the tube and the slide or tile technique. The use of slides is a much quicker method and more economical of material than is the tube technique. A further advantage of slides is that they can be examined microscopically without disturbance of the sediment. Slides or tiles can be used to best advantage only when very potent serum is available; their use is not advocated for the detection of anti-Rh agglutinins. In comparative tests, there was not any difference in agglutination on slides at 37° C. and at room temperature.

Physical and chemical changes

Sedimentation of red cells

Standardization of sedimentation rate.—Cutler presents a paper with the avowed object 'to discuss briefly the important factors known to have a determining influence on sedimentation rate, the basic principles involved, and to call attention to a new technique . . . (which) takes for its starting point the observation that it is the size of the rouleaux which ultimately determines the rate of settling'. The sedimentation rate is subject to the Stokes physical law regarding the sinking of particles suspended in a fluid medium. The equation is $V = \frac{2}{9} \frac{S - S_p}{\eta} r^2$, when V is the velocity of the fall, g the gravitation constant, S the specific

gravity of the erythrocytes, S_p the specific gravity of the blood plasma, η the absolute viscosity of the plasma and r the radius of the erythrocyte aggregates. It will be noted that the right side of this equation contains four variables. Cutler declares his general acceptance of Stokes's equation in the case of blood sedimentation but points out that before the formula becomes applicable time has to be allowed for the aggregates or rouleaux of erythrocytes to form. He further states that the arrangement of the erythrocytes in rouleaux and the size of the rouleaux are essentially functions of the plasma and are specific for the different plasma and that the size and number of the individual cells are of no consequence. In ordinary sedimentation tubes however the packing of the cells in the lower part of the tube interferes with the velocity of the fall of the rouleaux. Therefore the value of sedimentation as an index of the condition of the blood plasma is to be found in the period of maximum velocity of fall and there only. Cutler then describes his technique for ascertaining the maximum velocity of sedimentation which essentially consists in taking readings every 5 minutes and plotting the result on square paper, each square representing 5 minutes vertically and one millimetre horizontally. The greatest drop in any 5-minute period is the maximum sedimentation rate. Allowance has to be made for length of tubes; the cells fall faster in long tubes than in short ones. In the Cutler tube a maximum rate of 1 millimetre in 5 minutes is normal; anything higher is pathological.

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BLOOD PRESSURE, HIGH AND LOW

See also B.E.M.P., Vol. II, p. 503; and Cumulative Supplement, Key Nos. 170 and 171.

Physiological blood pressure

Influence of respiration

Intra-arterial pressure.—Battro and his colleagues have studied the influence of respiration on the blood pressure by registering the intra-arterial pressure of human subjects. They used a Hamilton manometer with a rubber membrane and having a natural frequency of from 60–80 oscillations per second. The calibration was made before and after each reading of blood pressure. The pressure in the system was measured according to the blood pressure of the subject. The respiratory movements were simultaneously registered by pneumograph. The authors found two sets of waves. (1) Vasomotor waves which were independent of respiration.

They appeared either during normal breathing or during brief periods of apnoea. (2) Waves which coincided with and depended upon respiratory movements. The respiratory waves had a rhythm synchronous with that of respiration. The authors conclude that intra-arterial pressure has no uniform behaviour during the respiratory movements, but varies with the type of breathing (thoracic or abdominal) or with the frequency or depth of respiration. They found that with deep thoracic breathing there is an increased pressure during expiration and a decrease during inspiration. There was inspiratory elevation during abdominal breathing. At the beginning of inspiratory apnoea and of the Valsalva test there was a fall in blood pressure. During expiratory apnoea there was a slight fall at first and a rise at the end. The sharp rise of intra-arterial pressure caused by coughing was accompanied by an increased intraspinal pressure.

Clinical estimation of blood pressure

Influences on variation

Personal experiments.—As he had previously found that congestion of an extremity tended to increase in it the diastolic blood pressure, Gambill reports that he contrasted the blood pressure in his limbs before rising in the morning and before retiring at night. Since healthy legs are known to swell more on hot days than on cold ones he studied the seasonal variation of his blood pressure, using a pneumatic cuff especially designed for the thigh and an ordinary cuff for the arm. During summer his diastolic blood pressure was always several millimetres of mercury higher in the morning than it was in the evening; the difference was greater in the thigh in which, when in the horizontal position, the pressure averaged 24 millimetres. There was less diurnal variation in winter in the thigh and practically none in the arm. In summer the systolic blood pressure in both the arm and the thigh was about 10 millimetres higher in the morning than it was in the evening. During winter there was practically no diurnal variation in systolic pressure. The pulse rate increased during the day and the maximal variation was 34 beats per minute in summer and 14 beats in winter.

High blood pressure

Essential hypertension

Aetiology.—The claim that diethylstilboestrol (stilboestrol) can produce hypertension in rats is not upheld by Matthews, Emery and Weygandt. Groups of 45 castrated female and 35 normal male rats were given one milligram of the sodium salt of diethylstilboestrol daily by stomach tube for periods of from 4 to 100 days. Comparable groups of untreated rats served as controls. Both direct and indirect methods were used to determine blood pressure. The indirect method gave consistently higher values. No deviation from the normal range of values determined in the controls was observed; heart rate and respiratory rate were unaffected.

Importance of renin.—In his Oliver-Sharpey lectures Pickering treats of the circulatory disturbances underlying arterial hypertension. By far the commonest condition of which raised pressure is a symptom is that known as essential hypertension. Here the raised arterial pressure is not due to increased output of the heart or to increased blood viscosity; both have been measured and found to be normal. The cause may therefore be inferred to be constriction of the vessels at some point in the circuit and measurements of the pressure at various points lead to the conclusion that the site of the narrowing is in the small arteries and arterioles. Increased rigidity of the main arteries may be dismissed as an aetiological factor, because on theoretical grounds it can lead only to increased pulse pressure and cannot affect mean arterial pressure. Two kinds of structural change have been observed to occur in the small vessels. These are (1) fatty and hyaline thickening of the tunica intima, found in about 98 per cent of patients with essential hypertension in the renal (especially the afferent glomerular) arterioles and less frequently in other organs; (2) the condition known as necrosing arteriolitis (Fahr) in which masses of granular material appear in the tunica media or intima, a condition which is always present in the kidney and sometimes elsewhere in the malignant type (never in the benign type) of hypertension. Evidence that these structural changes are the result, not the cause, of essential hypertension is furnished by the normal dilator and depressor responses to the usual tests. The chief factor appears to be spasm, and experimental work suggests (1) that this is of humoral, not of nervous, origin and (2) that it affects the efferent glomerular arterioles of the kidney chiefly, the vessels supplying the voluntary muscles little if at all and the cutaneous and cerebral vessels slightly. A similar agent appears to be responsible for the hypertension of aortic coarctation. In acute nephritis the available evidence suggests that the hypertension is of different, possibly of nervous, origin. In pregnancy toxæmia the circulation presents some features similar, others dissimilar, to those of acute nephritis. The nature of the chemical substance assumed to be concerned in hypertension is at present uncertain. Except in the rare paroxysmal hypertension associated with phaeochromocytoma adrenaline can be ruled out with some confidence; witness the red face of many patients with hypertension and the normal paling in response to intravenous injection of adrenaline. The agent probably responsible is renin, an enzyme produced in the kidney, which acts upon a body, hypertensinogen, present in plasma to produce a pressor substance, hypertensin. The author propounds the theory that renin is released from the kidney when for any reason intraglomerular pressure falls, but little evidence from human sources, for or against, is as yet available.

Results of sympathectomy.—Ayman and Goldshine report observations made over a period of 6 years up to 1943 on a well-controlled group of 14 patients, under 50 years of age, with essential hypertension which had been treated by sympathectomy. Blood pressure readings

were taken at the start of, during, and after 20-minute rest periods at the clinic, and also at home by the patients themselves before and after operation. One patient died a few days after operation. There were 2 patients with papilloedema, 2 with angina pectoris, and 4 with cerebral haemorrhages before operation. There was only one case in which renal failure was found. The heart was not much enlarged in any patient. In the earlier patients, the operation was that of bilateral supradiaphragmatic splanchnicectomy and dorsal ganglionectomy. Lumbar ganglionectomy was added in later cases, and finally bilateral transdiaphragmatic lumbo-dorsal splanchnicectomy was carried out. The chief symptom relieved was headache. In one case symptoms increased after operation. Four patients who had been almost wholly incapacitated returned to full activity after operation. In 3 patients the more extensive sympathectomies resulted in a fall in blood pressure to the normal, which has been maintained for nearly 5 years of observation. Five patients failed to respond to less extensive sympathectomies and one patient did not respond to an almost total sympathectomy. The authors conclude that the criteria for sympathectomy are severe or progressive disease in which there is not any renal or heart failure, and the development of any of the following: cardiac enlargement, electrocardiographical evidence of left ventricular strain, albuminuria, marked changes in the fundi.

Other forms of hypertension

Relation to renal disease.—Eighty-five cases with previous renal trauma in the records of the Mayo Clinic are reviewed by Braasch and Strom in order to ascertain the relation of renal trauma to hypertension of unilateral renal origin. Thirty-five cases were excluded from further study; of the remaining 50, the patients who had a history of injury to a presumably normal kidney, had had their blood pressure recorded at some time during their attendance at the Clinic and the records show that in some cases hypertension had existed prior to the injury. Nephrectomy was necessary in only 5 of these 50 cases as the authors have found that conservative treatment of a renal injury usually results in recovery. In 3 of the 5 cases there was hypertension and after nephrectomy the blood pressure returned to the normal; in the 2 remaining cases the pre-operative blood pressure was normal. From a study of 38 of the 45 patients who were not operated on the authors conclude that hypertension does not always follow upon changes in the kidney after trauma. Certain types of pathological change may result from renal injury and may thus produce hypertension, usually in cases in which there is secondary renal infection. The hypothesis is borne out by the fact that in most renal lesions which produce hypertension, kidney changes secondary to chronic infection have been found. The authors mention one exception, a patient with hypertension who had not secondary infection but who had an encapsulated haematoma which was compressing the kidney. Before kidney trauma is decided upon as the cause of the hypertension it is important that the blood pressure and clinical history of the patient before the injury should be considered.

Renal disease and D.O.C.A.—Selye, Hall, and Rowley, of McGill University, Montreal, report on the results of experimental research into the production of vascular lesions on the kidneys and pancreas by treatment with desoxycorticosterone acetate and sodium chloride. The research was carried out on young albino rats and bears out that the effects of desoxycorticosterone acetate (D.O.C.A.) and sodium chloride in the treatment of Addison's disease are adverse. Four groups of young albino rats were treated as follows. (1) Those in the first group were given twice daily hypodermic injections of 3 milligrams of D.O.C.A. in the form of crystal suspension in one cubic centimetre of water; after a month's treatment the amount of D.O.C.A. given was raised to 5 milligrams. (2) Those in this group had the same treatment as those in (1) but 1 per cent of sodium chloride was used instead of ordinary tap water. (3) These rats received sodium chloride and cholesterol in the same amount and manner in which D.O.C.A. was given in groups (1) and (2). As cholesterol has not any hormonal properties but possesses the sterol nucleus it was considered that the rats thus treated with this compound would act as injected and sodium chloride controls. (4) The animals in this group acted as entirely untreated controls. On the fifty-third day all the animals were killed and their organs were kept for histological examination. Even to the naked eye the kidneys in group (2) were clearly abnormal; the surfaces were irregular and had a flea-bitten appearance. Prominent cardiac hypertrophy was present in all the animals in group (2) and the pancreas was extremely oedematous. Histological examination of the kidneys showed that they were only slightly affected in group (1) and remained normal in groups (3) and (4) but in group (2) they showed the features of malignant nephrosclerosis; the glomerules were enlarged and showed capsular fibrosis, advanced hyaline changes in capillaries of the glomerular tubes and advanced degeneration in the afferent glomerular arteries, with necrotic changes in the walls in many cases. The experimental disease thus produced bears a striking resemblance to the hypertensive heart disease of renal origin as seen in man.

Treatment

By potassium thiocyanate.—D'Silva and Evans discuss the treatment of arterial hypertension with potassium thiocyanate. Twenty-five cases were treated. The drug was given in doses of 0.1 gramme thrice daily and blood estimations were made. At the end of a week, if the serum thiocyanate concentration was below 4 milligrams per cent, the same dosage was continued and after a further week was increased provided that no great increase in the blood level of the drug was noted; a weekly increase of 0.4 milligram was added until a blood

level of from 5 to 12 milligrams was obtained. If after the first week the serum thiocyanate was from 4 to 11 milligrams the second week's dosage was reduced to 1.4 grammes weekly. It was later modified in accordance with the serum thiocyanate concentration. In cases in which after the first week of medication the blood showed a level over 11 milligrams per cent, the dosage was reduced to 0.4 gramme weekly and thereafter altered cautiously. After the patients were discharged from hospital periodic blood examinations at shorter intervals were carried out. No selection of patients was made. Eleven responded by a fall of 40 millimetres or more in systolic pressure and 20 millimetres or more in diastolic pressure. Six others showed smaller falls in blood pressure and 8 showed no fall. In all the patients who had responded well to 2 weeks' treatment no alteration in their improvement occurred after they were allowed out of bed. In 7 of these the dosage of potassium thiocyanate was reduced to low levels with a consequent fall in the serum concentration, and in all the blood pressure returned to its original level. Subsequent increase failed in one case only to result in a further satisfactory response. Headache was relieved in 14 out of the 17 cases in which it was a symptom and vertigo and lack of concentration were relieved in a large proportion of the cases. In 2 cases toxic effects were observed—tiredness, nausea and limb pains. The authors conclude that this mode of treatment is a symptomatic remedy and a valuable adjunct, but that it does not alter the course of the underlying disease.

Thiocyanate and histamine therapy.—Occasional distressing effects have been observed as a result of the use of thiocyanate in the treatment of hypertension. Odel and Horton advocate the use of histamine in order to counteract such disadvantages. Toxic manifestations have usually been imputed to overdosage, cumulative effect and idiosyncrasy. Regulation of concentration in the blood rather than of dosage has been recommended, nevertheless toxic effects have followed low concentration and minimal dosage. The authors' 3 cases illustrate anginal pain and dyspnoea complicating thiocyanate therapy. First, in a woman aged 38 years who reported 17 years of hypertension, diffuse arteriolar disease was diagnosed. Bilateral lumbar sympathectomy gave only transitory benefit. Daily administration of potassium thiocyanate produced within 3 days vomiting, dermatitis and anginal symptoms. Later, on recourse to intravenous administration of histamine diphosphate, a dilution of 1 in 250,000 of physiological saline solution was introduced at 200 drops per minute. This administration which lasted for 50 minutes was repeated 4 times in a fortnight, the blood pressure dropping progressively with each treatment during administration. Surprisingly, a return to administration of potassium thiocyanate produced no untoward symptoms. Although discomforts necessitated intermissions from the drug the patient was able to take thiocyanate daily with 9 tablets of histaminase, for 17 months, during which time she had relief from hypertension. Previously intolerant of a concentration of 2 milligrams she then tolerated 9.6 milligrams of thiocyanate per 100 cubic centimetres of blood. Recurrence later of untoward symptoms compelled discontinuance. A second patient of like diagnosis and like intolerance received histamine in March 1940. Two years later he continued to take thiocyanate with benefit and without discomfort. In the third case histamine although less effective made possible the taking of potassium thiocyanate over longer periods.

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BLOOD TRANSFUSION

See also B.E.M.P., Vol. II, p. 530; and Cumulative Supplement, Key No. 172.

Selection of donors

Care of donors

Fainting of blood donors.—The condition of fainting, immediate and delayed, in blood donors has been investigated for the Medical Research Council. 'Fainting' was regarded as including the occurrence alone or in combination with pallor, feeling of warmth, dizziness, sweating, nausea, epigastric discomfort, blurred vision, restlessness, feeling of cold, unconsciousness, vomiting and convulsions. These symptoms are cited in the order in which they occurred most often. When a donor or two consecutive donors fainted, the successor or two successors were taken as controls, all being patients of the same operator. The fainting rate (that is, number of persons who fainted divided by number of persons bled) approached 5.5 per cent. Men were slightly less prone to faint than were women and although age is intrinsically unimportant spinsters showed a less tendency to faint than did married women. Occupations were classified as clerical, factory, housewives and others. Differences between controls and fainters did not emerge except that clerically employed spinsters over 35 years of age were

prone to faint. Posture at work, whether standing or sitting, proved to be immaterial. If a long wait before being bled was disadvantageous to the apprehensive, it was a benefit to those who arrived exhausted. Possibly a fast exceeding 6 hours in length will tend to produce faintness. Inquiries concerning menstruation indicated that the latter half of the cycle was the best time for the donor. Occasional difficult bleeding was not found to be an important factor in the occurrence of fainting. First donations were slightly more liable to cause faintness than were subsequent donations; fainting on one occasion was often associated with previous faints at donation. Of fainting donors the notable percentage of 44 gave a history of syncope in other circumstances. The onset of faintness at venepuncture, during bleeding, at withdrawal of the needle or while resting was noted but did not prove to be informative. Record cards completed and returned by 4,212 donors showed an incidence of delayed faintness of 1.2 per cent in men and 1.8 per cent in women. In both groups consciousness was lost in less than 1 per cent of cases. The findings suggest that when the need is less urgent prospective donors prone to faint should not be called upon to donate blood.

Technique of transfusion

Methods

Gelatin solutions.—The use of gelatin in intravenous transfusion has been studied by Brunschwig, Corbin and Johnston in experiments on dogs and on human beings in order to ascertain whether or not the gelatin is well tolerated and whether or not it can be utilized metabolically. A specially prepared 10 per cent sterile solution of gelatin was used, and preliminary experiments were made on dogs, which were kept on a low protein diet. All the injected gelatin did not appear to be excreted immediately and the urea excretion was increased, indicating that some of the gelatin was katabolized. In human subjects, trial intravenous injections of 10 per cent gelatin solution did not provoke any reactions, but when larger amounts were injected into several patients chills and fever were observed in one case. In 5 patients with malignant disease and in one patient with a fistula of the small intestine some of the gelatin appeared to be retained and utilized in the body. It is pointed out however that gelatin is an incomplete protein and does not provide all the essential amino-acids required by the body tissues. Gelatin also varies in quality but some types are well tolerated and do not induce hypersensitivity. The intravenous administration of gelatin may be of some practical value, if the other essential amino-acids can be given parenterally or by the mouth.

Apparatus and procedure

Viscose tubing versus rubber tubing.—The modern technique of blood transfusion dates from the introduction of sodium citrate as anticoagulant by Lewisohn in 1915. Despite the care devoted to blood grouping which eliminated the risk of intrinsic reactions arising from the infused blood, febrile reactions occur in from 1 to 10 per cent of infusions with citrated blood. Naftulin, Wolf and Levinson believe that these reactions arise from three sources: (1) pyrogenic substances in distilled water, (2) impure chemicals used for preparing solutions and (3) improper or inadequate cleansing of the equipment used. In this paper the authors deal with the last-named cause. They consider that rubber tubing has inherent defects. New tubing has to have the sulphur and other impurities with which it is covered removed in order to render it pyrogen-free and once it has been used there is no certainty that all residual protein material has been removed from the lumen of the tubing. On the other hand rubber tubing after efficient cleansing can be used repeatedly for the administration of dextrose and saline solutions which do not contain protein. For these reasons all infusions of whole blood, plasma and serum at the Michael Reese Hospital, Chicago, are now administered through specially prepared thick viscose tubing which is cheap to manufacture and can be discarded after use. It has however certain physical disadvantages. In a total of 1,137 blood transfusions given through viscose tubing the incidence of pyrogenic reactions was 0.64 per cent; the authors claim this to be a material decrease as compared with the reaction rate encountered when rubber tubing is used.

Indications for transfusion

General principles

The transfusion of blood and blood derivatives in emergency conditions is discussed by Vaughan. As a result of recent observations it is now thought advisable that, in order to prevent renal impairment, any severely injured patient should be treated as soon as possible by transfusion regardless of the blood pressure. It has been found that elderly persons with myocardial degeneration or with hypertension tolerate transfusion well. Serum and plasma have been found to be adequate for immediate transfusion after injury. Late transfusion (within 24 hours of injury) may be often required also since anaemia is a common sequel especially to severe burns; stored blood appears to be efficacious for the purpose. When large numbers of patients require transfusion the use of blood derivatives will eliminate the necessity of preliminary cross-matching. Dried preparations are preferable to fluids since they are always sterile, the concentration of protein can be varied and different diluents can be used. In cases of burns haemoconcentration is generally present and a twice concentrated blood derivative can be used to replace the fluid loss and to combat oedema in the burned part. The dosage and the choice of derivative varies in the case of each patient. A case should not be regarded as hopeless until at least 3 litres have been given without any clinical response—there is little risk of overdosage. In repeated late transfusion therapy daily blood counts,

haemoglobin determinations and protein estimations must be made. When anaemia ensues in cases of burns transfusions of whole blood may be required to be given at intervals for several weeks. After the first 24 hours transfusions should be given by the slow drip method. In cases of extensive burns the fluid may be given by the sternal route since it may be impossible to utilize a vein.

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BONE DISEASES

See also B.E.M.P., Vol. II, p. 553; and Cumulative Supplement, Key Nos. 175-184.

Osteitis deformans (Paget's disease)

Clinical picture

Normal serum calcium and serum phosphorus.—Miller reports a case of Paget's disease in a woman aged 73 years. She was one of a family of four sisters and two brothers and all four sisters were the subjects of osteitis deformans. A point not hitherto recognized in such cases is the association of arterial sclerosis of the Mönckeberg type with calcareous deposit in the muscular media and necrosis and cystic formation in the affected bones. In the case reported the levels of serum calcium and serum phosphorus were normal, which is remarkable in view of the considerable destruction of bone going on and of the arterial calcification in the muscular media. The author confirms the existence of 2 forms of osteitis deformans, (1) the monostotic common form, confined to one bone in the skeleton and (2) the rare polystotic form, involving several bones or the greater part of the skeleton.

Osteoclastoma (non-malignant giant-celled tumour; 'myeloid sarcoma')

Morbid anatomy

Aural polypus with myeloid characteristics.—Lord and Stewart report the third authenticated occurrence of an osteoclastoma in the temporal bone. The bones of the skull, with the exception of the mandible and the maxilla, are rarely affected. A woman of 50 years of age had tinnitus in the right ear in March 1939; subsequently unsteady gait developed. An aural polypus removed in July was not microscopically examined. A recurrent polypus removed one year later showed the multinucleated giant cells of an osteoclastoma embedded in a stroma of spindle cells. Radiological examination showed bone destruction involving the mastoid process and invading the squamous portion of the temporal bone and the occipital bone. Partial removal only was found possible at operations in June and in July 1940, and a 6.6 milligram radium needle was inserted for a period of 96 hours. Later the radium beam and deep X-ray irradiation were employed and progress was locally and generally satisfactory until October 1941, when dysphagia developed. This was due to a swelling in the right lateral nasopharyngeal wall which pushed the tonsil and soft palate towards the middle line. Gradual deterioration led to death, after 3 years' observation, in May 1942. At necropsy, the osteoclastoma was seen to have invaded the petrous and mastoid portions of the temporal bone, the sphenoid and ethmoid bones and the sella turcica. There was invasion of the posterior fossa of the skull, erosion of the dura mater and encroachment on the cerebellum. Metastases were absent and microscopically the features as before were those of a benign giant-celled tumour, myeloid sarcoma of Paget or osteoclastoma.

Acute osteomyelitis

Treatment

With penicillin.—Williams and Nichols report 2 cases of osteomyelitis of the frontal bone which yielded to treatment with penicillin. Facial and cranial osteomyelitis may terminate speedily in fatal meningitis; in the localized form the lesion heals spontaneously. A third variety, initially acute, inevitably invades the bone marrow and produces subperiosteal and epidural abscesses. To this type, known as Potts' puffy tumour when it invades the frontal bone, these 2 cases conform. In a boy who complained of ocular pain pyrexia developed, with delirium and loss of sphincteric control. Blood culture showed the presence of *Staphylococcus aureus*. A midfrontal swelling appeared. The administration of sulphadiazine proved to be ineffective during a fortnight's treatment. At the Mayo Clinic radiography showed right-sided general sinus infection. By continuous drip method the patient received 473,000 Oxford units of penicillin during a fortnight; the blood culture became sterile in 72 hours. The frontal abscess refilled after incision and deeper exploration evacuated, as often happens, a large epidural abscess. Rapid recovery ensued. The second patient, a man aged 35 years, had a left maxillary chronic sinusitis which was drained by making a naso-antral window. Two inflammatory recurrences in the malar bone, from which anaerobic short-chain streptococci were cultivated, yielded temporarily to incision and to instillations of zinc peroxide and sulphadiazine. In a third recurrence which ensued in the malar, nasal and frontal bones, penicillin was again employed with immediate and permanent benefit.

Tumours of bone**Malignant**

Ewing's sarcoma: pathology and radiological aspect.—Ewing in 1921 depicted a tumour of bone marrow originating in the vascular endothelium. Stout, doubting its endothelial origin, agrees with Oberling that it is a reticulosarcoma. Swenson considers the radiological aspect. An analysis of the data of 26 cases or records and 16 pathological specimens—42 items all told—published from the Surgical Pathology Laboratory of Columbia University, and covering the period 1906–43, shows that Ewing's tumour is one which affects chiefly the shafts of long bones, and which has cells mostly structureless but which sometimes resemble immature erythrocytes, reticulum cells and capillary endothelial tubes. Clinically males are more often affected than are females; the ratio is 3 : 2. Neither youth nor age is exempt but 63·2 per cent of patients were under 30 years old. The growth, starting endosteally, soon invades surrounding tissues. Metastatic growths are blood-borne and usually select the lungs, bones or brain. Radiographically, pathognomonic features are lacking and supplemental biopsy is desirable; malignancy however is rarely in doubt. The tumour is not itself osteogenic but stimulates bone formation; a laminated deposit of bone resembling onion skin is considered to be characteristic of Ewing's tumour. This deposit was present in 4 only in a group of 26 cases, the predominating feature in 22 cases being bone destruction. For purposes of X-ray irradiation the entire bone was regarded as involved. A cross-fire application was adopted when possible in variable daily doses, 4,500 r being aimed at as a maximum. Irrespective of treatment, prognosis is grave. Of the 26 patients, one, who represents outstanding therapeutic success, is alive 32 years after amputation of the femur. One patient who showed an affected vertebra is alive and well after 6 years and one patient, whose humerus was involved and who received irradiation only, died 6½ years later of pulmonary metastasis. Three surviving patients are too recently treated for comment on their cases to be of value. The remaining subjects succumbed after an average survival period of 15 months.

Necrosis**Kienböck's disease**

Clinical picture.—Gordon records 2 cases of Kienböck's disease of the semilunar bone. This is not rare and is generally regarded as belonging to the same class of disease as Köhler's disease of the tarsal scaphoid, Calvé's disease of the spine and Perthes's disease of the head of the femur. But whereas these, essentially epiphyseal in origin, are found in children, Kienböck's disease is found only in adults; Gordon's 2 cases were in men aged 30 and 33 years respectively. The typical case shows a syndrome consisting of pain over the semilunar bone, limited movement of the wrist, possible ultimate retraction of the head of the third metacarpal bone and degeneration of the semilunar bone which can be seen in radiographs. Most authors agree that the condition is fundamentally an avascular necrosis but opinion about the aetiology is divided. The possibility is suggested that bacterial infection is an aetiological factor in all cases not directly attributed to injury.

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BRAIN: REGIONAL DIAGNOSIS

See also B.E.M.P., Vol. II, p. 609; and Cumulative Supplement, Key No. 188.

Disorders of function produced by disease or injury**The electroencephalograph**

Present-day uses.—MacMahon presents the present-day position of electroencephalography. The variations in potential are much smaller than are those in electrocardiography as they are measured in microvolts and endure from $\frac{1}{1000}$ to $\frac{1}{10000}$ of a second. An amplifying system is employed for the purpose of measuring the waves, which are further reduced in their passage from the brain to the electrodes. Different parts of the brain are tested simultaneously. In the normal subject whose eyes are closed and who is refraining from mental activity the alpha or Berger rhythm can be recorded; the rhythm may however be absent or minimal in a number of normal subjects. The rhythm consists of rhythmic oscillations of a frequency of from 8 to 14 per second; it apparently originates from the post-central cortex. In a state of drowsiness the rhythm is exaggerated, in light sleep faster waves with alpha characteristics may appear paroxysmally and in profound sleep frequencies of less than 6 are found. Alcohol and drugs which depress the higher centres produce an initial heightening of the alpha waves, which subsequently disappear. Difficulties in obtaining cooperation vitiate the results in children. Beta and gamma waves have been described but many consider them to be artefacts. An 'automatic analysis' has been devised by Walter. Twenty reeds, each tuned to a frequency in the 1 to 20 cycles per second range, are energized by the output of the electroencephalograph. Each reed resonates as an entity and indirectly actuates the analyser ink writer. The length of time during which a reed vibrates is determined by the amplitude and number of vibrations which occur in a certain pre-determined 'epoch'. Under

such conditions potential is built up and recorded during the epoch in which it occurs. Waves of considerable potential and a frequency of from 1 to 6 cycles per second have been described as delta waves. These are used successfully for localization of cerebral neoplasms; they do not emanate from the new growth but from the disturbed contiguous cortex. If the tumour be deeply seated or if the intracranial pressure be very high localization is difficult. Other space-occupying lesions and abscess of the brain may be similarly detected. Nearly all *grand mal* cases of epilepsy have a delta focus in the frontal gyri which also may be demonstrable between fits. During *petit mal* attacks there is a spike and wave pattern of great amplitude; in the inter-paroxysmal period the discharge is delta in type. The older the patient is the less likely are electroencephalographical abnormalities to be found. There would appear to be a large proportion of potential epileptics among children, especially among those who show behaviour problems. Criminal psychopaths have shown a very considerable percentage of delta type potentials.

MacMahon, J. F. (1944) *Med. Pr.*, **211**, 230, 253.

BRAIN TUMOUR

See also B.E.M.P., Vol. II, p. 619; and Cumulative Supplement, Key No. 189.

Special methods of examination

X-ray examinations

Radiological appearances and pathology.—Addressing the Radiological Society of North America Boldrey discusses the relation between the pathology of brain tumours and the radiological appearances. (1) Supratentorial tumours include the following. (a) Gliomas, which may come to the surface but which rarely cause changes in the skull. Any may show calcification, sometimes visible only in stereoscopic radiograms. Pneumography usually shows a generalized ventricular shift due to oedema; sometimes air can be seen filling a cyst. (b) Meningiomas, the appearances in which correspond to the 5 recognized types and include erosion or proliferation of the overlying cranial bones and enlarged vascular channels. (c) Pituitary adenomas, which usually cause enlargement of the sella turcica. (d) Cranio-pharyngiomas, which often show calcification in addition to expansion of the sella turcica and erosion of the dorsum. (e) Pineal tumours, which may contain lime also; in angiomas lime may be deposited in the vessel walls, appearing as parallel streaks. (f) Cholesteatomas, which are visible in the X-ray only if they erode the skull. (g) Benign cysts of the third ventricle, which may appear in pneumograms outlined by gas in the ventricle. (2) Subtentorial tumours include gliomas of various types and perineural fibromas. In most cases ventriculography yields valuable clues to the type of growth, showing characteristic displacement of the ventricles. Calcification is difficult to observe in the posterior fossa. (3) Other intracranial tumours comprise (a) chordomas, which in pneumograms may be seen arising from the clivus or which may cause erosion of the basi-occipital and the basi-sphenoid, (b) secondary carcinomas, which often erode the skull and (c) intracranial aneurysms which are demonstrable by arteriography.

Boldrey, E. (1943) *Radiology*, **41**, 107.

BRAIN: VASCULAR DISORDERS

See also B.E.M.P., Vol. II, p. 641; and Cumulative Supplement, Key No. 190.

Cerebral anaemia

The fainting attack (vasovagal syncope)

Induced anoxia and its effects.—Rossen, Kabat and Anderson conducted investigations on the effects of acute arrest of the cerebral circulation in man, by means of a specially designed inflatable cervical cuff—the Kabat-Rossen-Anderson apparatus—held down to the lower third of the neck. This apparatus does not affect the respiratory tract. The pressure in the cuff rises to 600 millimetres of mercury within $\frac{1}{2}$ second and deflation can be controlled both by subject and investigator. The subjects used were 11 schizophrenic patients and 126 normal young male volunteers, aged from 17 to 31 years. No harmful effects were observed after repeated tests on these subjects. In the schizophrenics the cerebral circulation was arrested for 100 seconds and loss of consciousness, convulsions, marked cyanosis, involuntary urination and defaecation, bradycardia, dilation of pupils and changes in reflexes were noted. No lasting improvement in mental condition resulted. In normal subjects arrest of cerebral circulation for from 5 to 10 seconds caused fixation of eye-balls, blurring of vision, constriction of visual fields, loss of consciousness and anoxic convulsions. Recovery occurred quickly in every case and there was no danger attached to the procedure. The remarkable sensitivity of the function of the human brain to anoxia was demonstrated. It appears to be fairly constant in repeated tests in the same individual, but there is considerable variation from one individual to another. This variation appears to be due to differences in cerebral metabolism. The oxygen utilization of the human brain was calculated to be 1.56 cubic centimetres per second. In order to give the brain sufficient oxygen, the blood flow through it must average 1,400 cubic centimetres per minute. Although the brain represents only 2 per cent of the body weight, it receives, at rest, about one-third of the output of the left ventricle per minute.

Rossen, R., Kabat, H., and Anderson, J. P. (1943) *Arch. Neurol. Psychiat.*, **Chicago**, **50**, 510.

BRAIN: OEDEMA**Aetiology***Experiments on animals*

Histological findings.—Reid gives an account of cerebral oedema which occurs as a complicating factor in many intracranial and extracranial lesions. Experimental procedures were carried out on cats in order to reproduce oedema in the brain so that a clear histological picture might be obtained and in order to demonstrate that the changes seen were due to some other factor than that of excess tissue fluid. It was shown by these experiments and by investigation of cases in human beings that cerebral oedema can be caused by head injuries, operations or expanding lesions, by inflammatory lesions and by toxins originating in extracranial septic foci and by certain poisons. In cerebral oedema in human beings the gyri are flattened and the sulci become narrowed. The fluid in the subarachnoid spaces is diminished and the cut surface of the brain is moist and glazed in appearance. The perineural and perivascular spaces become widened and in severe illness the living cells of the choroid plexus swell slightly and the nuclei are seen to be eccentric. Changes are not observed in the axis cylinders, myelin sheaths, astrocytes, microglia, ependymal cells, connective tissue or meninges. The nerve cells are sometimes moderately swollen. In the region of intracerebral expanding lesions nearly all the cerebral structures are affected. The nerve cells and the axis cylinders are only slightly involved. The oligodendroglia and myelin sheaths become very much swollen and eventually rupture and undergo phagocytosis. Various astrocyte changes occur and the microglia are converted into granular corpuscles which become phagocytes. The blood vessels increase in number and the perineural and perivascular spaces are generally distended, the latter often being filled with compound granular corpuscles. The choroid plexus cells, ependyma and meninges do not usually show any change unless they are directly involved. The author concludes that the changes observed are obviously due to factors other than that of simple excess of intracerebral fluid.

Reid, W. L. (1943) *Aust. N.Z. J. Surg.*, **13**, 11.

BREAST DISEASES

See also B.E.M.P., Vol. II, p. 657; and Cumulative Supplement, Key Nos. 191–197.

Tumours and their treatment*Malignant tumours*

Carcinoma in young women.—De Cholnoky reviews 73 cases of cancer of the breast in patients under 30 years of age, the ages ranging from 12 to 29 years at the time of admission to hospital. A warning is given against conservative treatment based on the idea that cancer is so rare in the young as to be unlikely; 2 per cent of all mammary cancers occur in people under 30 years of age. One patient, aged 27 years, had been told by three doctors not to worry about the growth with the result that it was far advanced by the time she came under treatment. Early diagnosis can be made with certainty only by microscopical examination. All solid tumours of the breast should be removed. If the diagnosis is doubtful radical operation may be deferred pending the pathologist's report. Biopsy is misleading and dangerous. In the 73 cases 14 (19 per cent) were inoperable. Forty-nine patients were treated by radical operation; 20 (40·8 per cent) survived for 5 years, 6 (37 per cent) for 10 years. Results were best when the tumour measured less than 2 centimetres in diameter. These figures do not confirm the pessimistic view generally held concerning the prognosis of cancer of the breast in young subjects.

Metastases from cancer of the breast.—The incidence, clinical course and treatment of metastases from carcinoma of the breast are described by Freid and Goldberg. In a series of 641 patients 25 per cent had local recurrences after radical amputation of the breast. When there is diffuse involvement of the skin treatment is difficult and often useless. Localized lesions in the form of nodules are only slowly progressive and may be treated surgically or by X-ray irradiation. If ulceration and necrosis occur allantoin ointment or sulphathiazole ointment are beneficial and help to control infection. When the carcinomatous process involves the axillary glands radiotherapy is recommended and if glandular enlargement occurs in the opposite axilla biopsy should be made and the corresponding breast must be carefully examined. Invasion of the supraclavicular fossa is common in advanced cases and is generally associated with mediastinal or lung involvement; without generalized spread intensive irradiation may cause disappearance of enlarged supraclavicular glands. Among 168 cases of breast cancer 48 per cent showed skeletal metastases which if multiple can seldom be controlled. The records of fatal cases suggest that invasion of the lungs, pleura and mediastinum and of the abdominal organs nearly always occurs as the disease progresses; the rate of growth of the deposits may sometimes be reduced by radiotherapy. The literature contains few records of metastases in the central nervous system but one series of cases showed neurological evidence of brain involvement in 20 per cent of patients. The results of treatment by oöphorectomy for pelvic and systemic metastases have also been studied and although in some cases the primary breast tumour has regressed after oöphorectomy improvement has not been observed in patients with abdominal metastases. The elimination of oestrogenic stimuli by castration has produced striking improvement and prolongation of life in many cases of skeletal and intrathoracic involvement. The authors suggest that all patients

with breast carcinoma who have not reached the menopause should be castrated by X-ray irradiation.

Preoperative X-ray treatment in carcinoma.—The still unsettled question of the value of irradiation as a preliminary to operation for breast cancer is discussed by Dann and Koritschoner. The results obtained by them in a series of 7 cases treated in this way and in 5 additional cases treated by irradiation lead them to the following conclusions. (1) Complete destruction of all carcinoma cells in the breast and axillary glands is not attained by the technique employed, that is the delivery of fractionated daily doses of 100 r over a period of 10 minutes, the total dose depending upon the extent of the disease. In all but 2 of the 12 patients subsequent examination of tissues removed at operation or by biopsy revealed viable cancer cells. (2) Irradiation produces retrogressive changes in the tumour and decidedly reduces its size and may render operable growths previously regarded as inoperable. (3) It is not established that irradiation treatment improves the prognosis in operable cases. Two of the series of 7 patients have survived for over 5 years without evidence of recurrence. Four are dead, one is alive nearly 2½ years after treatment but is suspected to have a recurrence in the brain and one, who has been observed for only 9 months, is alive and well. One of the patients who at death had widespread metastases had had a simple mastectomy only. (4) Operable cancer of the breast should be treated by radical amputation. Radiation therapy is recommended for inoperable carcinoma and for operable growths when operation is refused or is contra-indicated by the patient's general condition. The authors comment on the apparently capricious effects of irradiation. For example, extensive areas of necrotic cancer cells may be found lying alongside well preserved tumour masses. This phenomenon however possibly is due to some other cause since it was noted in an untreated metastasis.

Carcinoma: X-ray therapy.—Gylstorff-Petersen analyses 582 cases of carcinoma mammae which came from various hospitals for X-ray treatment at the Aarhus Radium Centre, Denmark. Steintal's classification was adopted. Accordingly 147 patients were ranked in stage (1), 340 in stage (2) and 95 in stage (3). Of these groups the percentage survival after 5 years was 43, 27 and 4 respectively. Patients from the Aarhus Municipal Hospital received more immediate X-ray treatment which, with other factors, produced in stage (1) a better survival rate of 73 per cent. Post-operative irradiation was administered to 308 patients of stages (1) and (2), of whom 37 per cent survived for 5 years. Of 129 patients in whom recurrences were treated, 28 per cent survived for 5 years after operation. X-ray irradiation proved palliative but not curative in 113 inoperable cases, of whom 6 per cent survived for 5 years. Wide-field irradiation, additionally employed at first, was early discarded. For patients under 40 years of age the expectation of life exceeding 5 years is only one-half that of patients over that age. The malignancy of carcinoma increases from the benign form of Paget's disease through the colloid, intracanalicular, adenomatous, simple and scirrhous forms to the most malignant solid form. Glandular involvement is readily misjudged before and during operation. Marriage or parenthood does not affect prognosis. In stage (1) ablation of the breast with clearance of the axilla shows little advantage over ablation alone; in stage (2) the radical operation shows clear advantage; in both it is generally considered to be the operation of choice. Reports from other hospitals of pre-operative irradiation in stage (1) show a 5-year survival rate exceeding 50 per cent. This does not equal the post-operative 73 per cent of the Aarhus hospital for its own cases, but surpasses the rate of 37 per cent for patients from other sources radiologically treated at Aarhus. Dogmatic statement is difficult and the pre-operative treatment at Aarhus is too recently instituted to afford satisfactory evidence. Nevertheless pre-operative treatment is advocated.

Effect of stilboestrol.—Binnie describes 4 patients with malignant disease which arose in the breast, 3 of whom improved on X-ray therapy employed with concurrent administration of stilboestrol, and the fourth on administration of stilboestrol alone. The first patient had a pleural effusion and at least one lung metastasis. The second had multiple lung metastases and a pleural effusion. In the third a histologically proved carcinoma of the breast, which arose in the axillary tail and involved the axillary glands, improved steadily. The fourth patient was aged 76 years. She had a hard swelling of the left breast of 5 years' duration. It was the size of a man's fist and formed a fungating mass. She was given stilboestrol; the amount at first was 5 milligrams a day, later it was increased to 7 and finally it was reduced to 3 milligrams a day. The tumour regressed completely in 5 months' time and 3 months later the improvement was still maintained. Biopsy was not done and the Wassermann reaction test was not made. Binnie's impression is that stilboestrol is antagonistic to forms of malignant disease other than carcinoma of the prostate, and that if it is given in combination with irradiation, regression can be obtained which would not occur with the use of either treatment alone. The only discomforts which arose from the giving of large doses of stilboestrol were nausea and menorrhagia, and in one patient a generalized dermatitis which cleared when the drug was discontinued.

Binnie, G. G. (1944) *Brit. J. Radiol.*, **17**, 42.

de Cholnoky, T. (1943) *Surg. Gynec. Obstet.*, **77**, 55.

Dann, D. S., and Koritschoner, R. (1943) *Radiology*, **41**, 213.

Freid, J. R., and Goldberg, H. (1943) *Amer. J. Roentgenol.*, **50**, 499.

Gylstorff-Petersen, H. (1944) *Acta radiol., Stockh.*, **25**, 1.

BRONCHIECTASIS, BRONCHIOLECTASIS AND BRONCHIAL SPIROCHAETOSIS

See also B.E.M.P., Vol. II, p. 682; Interim Supplement, No. 19*; and Cumulative Supplement, Key Nos. 199–201.

Bronchiectasis

Aetiology

Haemophilus influenzae.—Finding that the routine bacteriological examination of bronchial secretion taken by bronchoscopic methods during a period of 5 years yielded a high percentage of *Haemophilus influenzae* in either pure or mixed culture, Allison, Gordon and Zinnemann decided to make further investigations. They were made on 288 patients who had attended the department of thoracic surgery in Leeds General Infirmary, either for an opinion concerning the advisability of surgical treatment or for diagnosis of some unexplained symptom or radiological appearance. Of the 288 patients, 100 suffered from bronchiectasis; *H. influenzae* was found altogether in 63 of these, in pure culture in 18, and predominating or in almost pure culture in 20. This suggests that *H. influenzae* is largely responsible for the occurrence of bronchiectasis, the essential nature of which is considered by modern authorities to be a destructive inflammatory process in the bronchial walls. Thirty strains of *H. influenzae* were tested by serological methods and only one corresponded to any of the Pittman types. The one strain agglutinated with type *e* serum (Pittman). A degree of virulence for white mice was shown by the respiratory strains which was less marked and less constant than that shown by the meningial types.

Part played by the common cold.—A study of 86 cases of bronchiectasis by Robertson disclosed 39 patients with infections of the nose or sinuses; the sputum in all was negative for tubercle bacilli. Among these 39 were 26 adults; 13 had maxillary antrum disease, one had ethmoid disease and 12 had nasal catarrh. The author emphasizes the great importance as an aetiological factor in bronchiectasis of the common cold with its sequela of chronic upper respiratory disease and urges that more attention be paid to prevention. Persons with colds should be isolated, or if they must go to work should be compelled to wear masks. It may be advisable in addition to attempt to sterilize the air of crowded rooms by using a mist of propylene glycol or by ultra-violet irradiation, if these methods are proved to be efficient and innocuous.

Sinusitis and bronchiectasis.—The evidence in favour of an aetiological relation between chronic or subacute sinusitis and infective disease of the chest is reviewed by McLaurin, who concludes that infection of the upper respiratory tract, particularly of the sinuses, must be looked upon as a constant menace to the lungs and as responsible for at least 85 per cent, and possibly 100 per cent, of all cases of chronic non-specific bronchitis, peribronchitis and bilateral bronchiectasis not due to pneumonia, lung abscesses or foreign bodies. An experiment carried out by the author showed that lipiodol (iodized oil) injected into the ethmoidal and sphenoidal sinuses in a conscious patient could be demonstrated radiologically in the bronchi 24 hours later. After 48 hours some lipiodol was still present in the smaller bronchioles. He argues that lipiodol is probably more irritating and therefore more rapidly expelled from the chest by coughing than is the mucopurulent discharge emanating from infected sinuses. Aspiration is therefore presumed to be of paramount importance as a mode of transference of infective material from sinuses to chest, although as other workers have shown the haematogenous or lymphohaematogenous route is responsible in some cases; spread by direct continuity is also a possibility. The importance of looking for chronic sinusitis in all cases of chronic intrathoracic infection, and treating it if present, is emphasized. None of the pathological conditions already mentioned responds permanently to any type of treatment unless the upper respiratory infection can be eradicated. Treatment thus requires the cooperation of the rhinologist, bronchoscopist, physician and surgeon.

The association of bronchiectasis with paranasal sinusitis has been noted by many observers and in a study by Simonton was observed 23 times in a series of 405 cases of sinusitis, that is in 5.7 per cent. Of these 23 cases, in 11 the onset of bronchiectasis was simultaneous with that of sinusitis. In 2 cases symptoms of sinusitis preceded the onset of productive cough; in 10 cases the history was not precise concerning which came first; in no case was bronchiectasis known to precede sinusitis. Eleven patients gave a history of antecedent pneumonia or of one of the acute diseases of childhood. These findings suggest that combined bronchiectasis and sinusitis are the joint results of some severe acute respiratory infection. The transference of infective material along the air passages provides for constant mutual reinfection. Treatment of chronic sinusitis when bronchiectasis is present is often vitiated in this way and cure cannot be expected unless the pulmonary condition is also treated. The author concludes that in cases in which both bronchiectasis and sinusitis are present and in which operation on the lung is considered to be suitable, radical treatment of the sinusitis should be deferred until the bronchiectasis has been dealt with.

Importance of middle lobe bronchus.—Brock draws attention to the practical importance of the middle lobe of the right lung. Radiographically a lateral view is essential in order to detect abnormalities of the middle lobe, which may be missed if reliance is placed upon postero-anterior films alone. The middle lobe bronchus arises from the anterior aspect of the right bronchus about 3 centimetres below the right upper lobe stem and almost at the same

level as the apical branch to the lower lobe which, if the middle lobe bronchus be regarded as arising at 12 o'clock, arises at 5 o'clock. The middle lobe bronchus is directed downwards and forwards for from 1 to 1·5 centimetres before it divides and is at first closely applied to the right lower lobe bronchus. It then divides into medial and lateral branches; the former supplies a quadrilateral, the latter a triangular, area of lung. The degree of separation of the middle lobe from the upper lobe varies; in about 10 per cent of cases the two are completely fused. The middle lobe bronchus is particularly liable to become obstructed as the result of tuberculous lymphadenitis. If the compression lasts for a long time permanent bronchiectatic changes are induced. Such a damaged lobe may remain quiescent for years and then become secondarily infected and produce symptoms and signs which often closely mimic malignant disease. Embolism of the middle lobe bronchus is relatively rare but does occur; secondary involvement by pneumonitis and abscess is not uncommon since the bronchus is well placed to receive septic material from other segments.

Clinical picture

Bronchiectasis and pulmonary tuberculosis.—As a secondary manifestation in pulmonary tuberculosis bronchiectasis has been regarded as a relatively benign complication, but Rilance and Gerstl bring evidence to show that in a small proportion of cases it assumes a position of much greater importance. They have collected a series of 35 patients in whom bronchiectasis appeared as the dominant factor in the clinical picture. Twelve other similar cases were verified at necropsy. The 35 patients were studied with lipiodol while they were undergoing sanatorium treatment and the bronchiectasis was thus discovered. In 3 the bronchiectasis was thought to be merely coincident; it was confined to one or both of the lower lobes; the tuberculous infiltration was present in one or both apices. Typical foul sputum and finger-clubbing were noted many years before any evidence of tuberculosis appeared. In the remaining 32 patients the bronchiectasis was thought to be secondary to the tuberculous process. Twenty-two of these patients, all sputum-positive, improved under treatment up to a point and in 17 the sputum became negative. Persistence of symptoms and signs prompted bronchographical investigation and the bronchiectasis was then discovered. In the 5 patients with persistently positive sputum despite apparently adequate healing as shown by X-rays, direct tuberculous involvement of the bronchi was probably the cause of both the bronchiectasis and the positive sputum. In all these cases the bronchiectasis became more prominent in the clinical picture as the tuberculosis receded. In the remaining 10 cases the outstanding features from the start were those of bronchiectasis. Despite the presence of clinical evidence of active tuberculosis and X-ray signs of cavitation, the sputum was persistently negative for tubercle bacilli. The importance of these cases lies in the fact that bronchiectasis in tuberculous persons may so closely simulate active tuberculosis as to be mistaken for it. Moreover the bronchial suppuration or its complications may cause death, as happened in 5 of the authors' total of 47 patients, of whom 3 had non-tuberculous metastatic abscesses and 2 had abscesses of the lung. Radiologically tuberculous bronchiectasis is often characterized by much distortion as well as dilatation of the bronchi.

Treatment

Treatment with sulphonamides.—In a series of 10 patients with bronchiectasis treated with sulphonamides Norris has compared the concentration of the drug in the blood with that in specimens of bronchial secretion obtained by bronchoscopy. When sulphadiazine was given by the mouth the average concentration in the bronchial secretion was about 60 per cent of that in the blood. Intrabronchial instillation of a 5 per cent suspension of microcrystalline sulphathiazole was carried out in 12 instances. The bronchial secretion examined 24 hours later was found to contain variable but considerable amounts of the drug and some was present after a period of 48 hours. When a 2·5 per cent aqueous solution of sulphadiazine, prepared by the aid of triethanolamine, was used none was found in the secretion 24 hours later. Clinically in all 10 patients a considerable diminution, averaging 69 per cent, took place in the daily volume of sputum; favourable alteration was noted in the bacterial flora. The author concludes that oral sulphonamide administration combined with bronchoscopical aspiration should be of distinct value as a preliminary to operation upon the lung in bronchiectasis. It seems worthy of trial also in cases considered to be unsuitable for surgical treatment. Instillation is not recommended because of the difficulty of ensuring equal distribution and continuous action.

The surgery of primary bronchiectasis.—For the purpose of illustrating the surgery of primary bronchiectasis Bradshaw and O'Neill select 76 cases of unknown causation. Unilobar lobectomy is relatively simple and has a low mortality, but unilobar bronchiectasis, apart from obstruction by a foreign body or in some other form, is rarely encountered. Bilateral lobectomy, up to the removal of 3 lobes, carries a mortality of 15 per cent whereas that of untreated bronchiectasis is 35 per cent. Time is well spent in ameliorating the patient's condition before operation by means of postural drainage, bronchoscopic aspirations, clearance of focal sepsis and blood transfusion. The pertinent value of sulphonamides is undetermined. Six weeks should separate the injection of iodized oil from the carrying out of the operation. Endotracheal oxygen-ether was usually employed in anaesthesia. Continuous spinal anaesthesia is an advantage if the cautery is to be used but the patient's comfort may not be complete. Individual ligation of the hilar bronchus and vessels of the lobe is ideal but often impossible. Occlusion of its bronchus and slight overinflation of the surrounding lobes

sometimes enables a line of demarcation to be found for dissection in a lobe but often the bronchial systems intercommunicate. After removal of the lobe, dusting of the hilar region with sulphanilamide powder shortens the period of drainage. In 24 patients the lower lobe was removed, and no visibly diseased tissue was left; there was one death. In 26 patients one lobe was removed, leaving known disease in other lobes; there were 4 deaths. In 17 patients 2 or more lobes were removed; 11 had unremoved disease in other lobes; 3 patients died. Of 9 pneumonectomies 4 were fatal; in all the cases disease was shown in the remaining lung. The operation is practicable; the high mortality and chronic invalidism of patients with untreated bronchiectasis encourage its use.

Results in combined chronic sinusitis and bronchiectasis.—Goodale reports the results of treatment in 65 cases of combined chronic sinusitis and bronchiectasis. (1) In 30 cases operation on the sinuses only gave the following results. Sinus symptoms showed pronounced or moderate improvement in 19 cases but slight or no improvement in 11; chest symptoms disappeared in one, showed pronounced or moderate improvement in 15 and slight or no improvement in 14. (2) Ten cases were treated by operation on the sinuses and lobectomy. Sinus symptoms disappeared in 3 and showed pronounced or moderate improvement in 7; chest symptoms showed pronounced or moderate improvement in 9, slight or no improvement in one. (3) In 14 cases lobectomy only was performed. Sinus symptoms showed pronounced improvement in 3, slight or no improvement in 11; chest symptoms disappeared in one, showed pronounced or moderate improvement in 11 and slight or moderate improvement in 2. The author advocates radical treatment of both the sinusitis and the bronchiectasis.

Allison, P. R., Gordon, J., and Zinnemann, K. (1943) *J. Path. Bact.*, **55**, 465.

Bradshaw, H. H., and O'Neill, J. F. (1943) *Surg. Gynec. Obstet.*, **77**, 315.

Brock, R. C. (1943) *Guy's Hosp. Rep.*, **92**, 82.

Goodale, R. L. (1943) *Arch. Otolaryng.*, Chicago, **38**, 148.

McLaurin, J. G. (1943) *Ann. Otol.*, etc., St. Louis, **52**, 589.

Norris, C. M. (1943) *J. Amer. med. Ass.*, **123**, 667.

Rilance, A. B., and Gerstl, B. (1943) *Amer. Rev. Tuberc.*, **48**, 8.

Robertson, A. N. (1944) *Med. Pr.*, **211**, 30.

Simonton, K. M. (1943) *Ann. Otol.*, etc., St. Louis, **52**, 598.

BRONCHITIS AND BRONCHO-PNEUMONIA

See also B.E.M.P., Vol. II, p. 696; Interim Supplement, No. 12*; and Cumulative Supplement, Key Nos. 202–207.

Broncho-pneumonia

Primary atypical pneumonia

Clinical picture.—Needles and Gilbert discuss their experiences of primary atypical pneumonia on the basis of 125 cases, with necropsy observations on one patient, the only fatality in the group. The prodromal features of ill health were present for only 1–3 days prior to admission to hospital, and resembled those of the onset of influenza. In their case reports rigor was shown to be uncommon and the usual initial symptoms were malaise, headache and anorexia. Cough occurred early in some cases but often it was not prominent; generalized body pains were usual. As the disease progressed all the symptoms were more severe although in mild cases they receded after from 3 to 6 days. A viscid light greyish-yellow, mucopurulent sputum was eventually produced in about half the number of cases; occasionally it was blood-streaked. There was neither frank haemoptysis nor rusty sputum. Cyanosis and dyspnoea were seen in the more severe cases and herpes labialis in 3 only. The temperature was remittent with levels rarely above 103° F. Physical signs were absent or minimal in contrast to the X-ray appearances in the early stages, but in the severe cases they were much more marked. The earliest changes detectable in the skiagrams were seen on the second or third day and took the form of a faint and usually localized exaggeration of the peribronchial markings, so that they had a streaked or linear appearance. The hilar markings were prominent. The markings at a later period increased in prominence and produced a mottled appearance; pleural thickening or exudate was rare. In many cases pneumoconiosis was simulated. Sputum examinations failed to reveal any single bacterial pattern in the disease; virus studies were not carried out. Leucocyte counts were usually normal or slightly above normal levels. Blood cultures did not yield any positive results. Treatment did not involve any specific measures. The authors stress the striking similarity of the symptoms and pathological changes of this disease with those of certain cases of influenzal pneumonia.

Van Ravenswaay and five other officers report on the clinical aspects of 1,862 cases of primary atypical pneumonia seen at the station hospital, Jefferson Barracks, Missouri, between 1st June 1942 and 10th August 1943. The disease was epidemic in character, and occurred in the first 45 days of the young soldiers' stay in barracks; the cause was undetermined. Five cases terminated fatally, a mortality of 0.26 per cent. During the same period 62 cases of pneumococcal lobar pneumonia occurred without a death. The observers regard the disease as an extension of an infection of the upper respiratory tract, headache, chill, fever, thoracic pain and cough developing in patients with a 'head cold'. Among the complications were pleural effusion 9.7 per cent, empyema 1.4 per cent, bronchiectasis 2.2 per cent. The X-ray films showed either a normal chest, increased bronchial markings in the affected area,

or a persistent shadow interpreted as 'unresolved pneumonia'. (The term, pneumonitis, is not used in the report.) The sputum was blood-stained in 24 per cent of the cases. The most constant physical signs were localized râles, either post-tussic or occurring at the end of inspiration. All patients in whom the temperature reached 102° F. were treated with sulphadiazine. Ammonium chloride was used as an expectorant, and sedative and narcotic cough medicines were avoided. Prolonged post-febrile rest in bed was found to shorten the rehabilitation period; the blood sedimentation rate with exercise tolerance tests were relied upon for the purpose of estimating progress and fitness for return to duty.

Acute pneumonitis in U.S. Navy.—Scott and Jones review the literature of acute pneumonitis and report on 74 cases observed during a period of 4 months at a naval air station in California. During 1940 the United States Navy reported 27,312 cases of what they term acute catarrhal fever, involving 140,698 sick days or an average of from 5 to 6 days for every case. From this catch-basket Scott and Jones would remove acute influenzal pneumonias and cases of acute pneumonitis. The latter condition is diagnosed when a localized area of pulmonary consolidation is demonstrated by chest radiography in patients with symptoms of an acute respiratory infection. The X-ray evidence is present within 48 hours of the onset of symptoms and often several days before abnormal physical signs can be detected. The usual appearance is that of a fan-shaped area of hazy density extending out from the hilar region in to the lower, or less frequently the mid-lung, field, lobular rather than lobar in distribution and becoming denser, larger and more sharply defined as the disease progresses. The density diminishes with resolution which may be completed within a week or 10 days; the symptoms often disappear before resolution is shown in the skiagram. Relapses are frequent and may be serious. The aetiology remains undetermined; most investigators strongly suspect a virus. Hornibrook reported an epidemic of 15 cases in which the *Rickettsia* of Q fever was isolated in 3 out of the 4 cases investigated. In the few fatal cases which have occurred the chief necropsy findings were haemorrhages and oedema. The disease is highly communicable and the incubation period has been variously estimated as from 7 to 20 days. The condition has little in common with true pneumonia and the symptoms of influenzal conditions are also absent. It is most likely to be confused with bronchial obstruction, tuberculosis, inflammatory areas around bronchiectasis, fungus infections and undulant fever. Treatment consists in rest in bed until a week after all fever has subsided. Sulphonamide drugs do not have any beneficial effect and may do harm. In this connexion the authors issue a warning against the indiscriminate and prophylactic use of these drugs, pointing out that in airmen they continue to produce anaemia, to lower the flying ceiling and to impair flying judgment for a long time after recovery from the infection.

Fresh data from seven hundred cases.—Primary atypical pneumonia is a communicable disease which is apt to occur when people are congregated, as in Army units. It has an incubation period of 1–3 weeks. In an analysis of 738 cases, Owen found the onset generally characterized by cough, succeeded by malaise and fever. Alternatively malaise preceded cough or onset resembled that of coryza. In half the number of cases on their admission to hospital the chest was clear, otherwise moist râles were frequent. Diagnosis within 24 hours was possible in 57 per cent of patients; in the remainder râles, diminished fremitus and breath sounds, or other signs, developed within a week. Physical signs, radiological findings and the severity of the disease showed a notable discrepancy. Fever reached its peak, averaging 102.8° F., within 48 hours of admission and the average duration of pyrexia (any temperatures exceeding 99° F.) was 7 days. Detention in hospital averaged 27 days but convalescence was prolonged. The pulse was full and respiration deep but neither was greatly accelerated. The pharynx was often injected and blood-streaked sputum was noted in 84 cases. Coughing was painful and slight epigastric rigidity was not uncommon. Radiography showed density spreading from accentuated hilar broncho-vascular markings, with definite predilection for the lower lobe. The average duration of consolidation was 19 days. An average leucocyte count of 9,000 per cubic millimetre constituted a leucopenia proportionate to the severity of illness. Treatment of the disease was symptomatic. Codeine gave partial relief to cough and malaise. Acetylsalicylic acid and other antipyretics effected falls in temperature but the discomforting diaphoresis and the erratic temperature curves produced by them, which tended to make estimation of the progress of the disease uncertain, discouraged their use. Steam inhalations occasionally relieved paroxysmal cough and the use of the oxygen tent was effective for cyanosis and dyspnoea. Positive benefit from the routine use of sulphonamide drugs was discredited, but they were employed in all severe and protracted cases. The *Pneumococcus*, *Streptococcus viridans*, *Rickettsiae* and various viruses have been suspected as causal agents but studies of sputum did not identify any specific organism. The military nomenclature of 'primary atypical pneumonia, aetiology unknown', stands at present.

Relation of the psittacosis virus.—Recent work in the field of virus research was the theme of the George Frederic Still Memorial Lecture given by Bedson at the University of London. The minute size of viruses, the difficulty with which they stain and the fact that they will not grow on non-living media contribute to the difficulty of studying them. In addition to touching on the relation of viruses to herpetic infections and to poliomyelitis the author dealt principally with primary atypical pneumonia. Primary atypical pneumonia is a disease which during the last 3 or 4 years has been recognized more and more often. The evidence available suggests that quite a number of different viruses are capable of producing the condition. Of

these the virus of psittacosis, although responsible for a comparatively small proportion of the cases, is the best known. It can be isolated by inoculation of mice with sputum but if this test cannot be carried out or is negative, indirect evidence may be obtained by means of the complement fixation test. The antigen employed is a heated saline suspension of virulent mouse spleen which is reliable and is safe in use. Work on these lines has shown that a virus can be antigenically complex and that psittacosis is much more widespread among various kinds of birds than was at first thought—so much so that it has been proposed that the word, ornithosis, should be substituted for psittacosis. Even this name however is not sufficiently comprehensive because the infection has been discovered in cats. The psittacosis virus is morphologically related to the viruses of trachoma, inclusion conjunctivitis and lymphogranuloma venereum, which all stain when Castañeda's method is used. Other Castañeda positive viruses have recently been isolated from man. Some of this group of viruses are susceptible to sulphonamides.

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BURNS AND SCALDS

See also B.E.M.P., Vol. II, p. 719; and Cumulative Supplement, Key No. 209.

Pathology

General features

Types of burn produced by various thermal agents.—Experiments were made by Elman and Lischer in order to study the nature of the burn lesion produced by various thermal agents. Burns in warfare and in civil accidents are mostly caused by hot water, oil or flame, and there is also the flash burn, which produces superficial injury that usually involves necrosis of tissue. In all, about 25 deeply anaesthetized dogs, whose hair had been previously removed, were used for the experiments. The methods employed were: immersion in hot water of varying degrees for varying periods of time, the ignition of a measured amount of petrol poured over the skin, and radiant heat produced by holding the tip of a cautery a few millimetres from the skin surface. The types of skin lesions which were produced were classified in three groups: (1) inflammatory reactions with oedema but no necrosis, (2) wet necrosis and (3) dry necrosis of the skin. (1) If the animal survived, the oedema subsided after 24 hours and left little or no permanent effects. (2) Wet necrosis manifested itself as a swollen moist necrotic area which rapidly became infected. Adrenal haemorrhage was observed with this type. (3) In dry necrosis the skin was hard and coagulated and tended to slough easily but there was not any infection. Although the type of lesion depended upon the duration of the burn stimulus as well as upon its intensity other factors also came in play, such as cooling of the skin by the blood flow and by radiation, and the presence or absence of pressure. The centre of a burn may be necrotic and its periphery show only oedema, as occurred when heated oil at 180° C. was poured over the surface of the torso.

Treatment

Advances in treatment

May chronicles the advances made in the treatment of burns. First, Churchill in 1921 emphasized the importance of fluid loss and haemoconcentration. Secondly, Davidson in 1925 introduced the effective use of tannic acid, although the theory of neutralizing toxins from the burned skin by precipitation was probably erroneous. Thirdly, in 1929 the toxæmic theory was replaced by the theory of infection from without, and triple dye, effective against both Gram negative and Gram positive organisms, was introduced. Plasma infusion is the fourth advance. Primarily, treatment is directed against shock by the use of morphine injection, by elevating the foot of the bed and by warm applications. Locally, sterile coverings are applied. Meanwhile infusion of plasma and 5 per cent dextrose in distilled water is prepared and is given continuously by the intravenous method. If plasma is not available whole or citrated blood, gum acacia or dextrose solutions may be substituted. The rate of intravenous infusion should not exceed 60 drops per minute. Formulas dictating the amount required are useful where laboratory facilities exist. Otherwise the area burned is estimated as a percentage of the body surface—head-neck 6 per cent, upper extremities 18 per cent, trunk 38 per cent, lower extremities 58 per cent—and 50 cubic centimetres of plasma are allocated to each percentage. Eschatin (a preparation of suprarenal cortex) up to 10 cubic centimetres given intravenously every 6 hours, or percorten (solution of desoxycorticosterone acetate) up to 4 cubic centimetres injected intravenously 4-hourly, are the adrenal extracts recommended. Control of shock must precede local treatment. After cleansing, and if possible the drying of the burned area with a hair dryer, the application of tannic acid and silver nitrate, of triple dye or of Vaseline gauze are the alternatives chosen. Sulphanilamide given orally, unless vomiting necessitates intravenous administration, is indicated. The sooner skin-grafting is initiated the less will be the deformity resulting from the burn. For the treatment of burns of the face, hands, feet, perineum and genitalia, ointments are better than

coagulants. The application of sulphanilamide ointment combined with cod-liver oil or of boric acid ointment are appropriate, and for the vulva constantly changed applications of gauze soaked in merthiolate (sodium ethylmercurithiosalicylate). Patients with minor burns which involve less than 10 per cent of the cutaneous surface may be treated as out-patients since general treatment other than the giving of a sedative for relief of pain is not required.

First-aid measures

Burns and scalds in children.—Burns and scalds in children under 12 years of age are caused mainly by domestic accidents. The social aspect of the injuries is emphasized in an analysis by Wilkinson of 366 cases admitted to the Royal Hospital for Sick Children, Edinburgh, between 1st June 1938 and 31st July 1942. The upsetting of a teacup, saucpan, kettle or teapot full of hot fluid is the chief cause; contact with unguarded fires and clothing set on fire by a lighted match also cause a large number of burns. Crowded living conditions and childish curiosity and thoughtlessness coupled with lack of adequate supervision rather than actual negligence on the part of the parents accounted for almost all of the cases. The peak of the time incidence of injury was reached in the early evening and that of the age incidence at the second year. The mortality rate, which was 4.9 per cent for the whole series, was highest among children in their first, fourth and fifth years; the effect of shock as a lethal factor was seen to be closely related to the extent of the injury. External first-aid remedies before arrival at hospital ranged from olive oil to vinegar; a dose of castor oil internally was given in 14 instances. Children whose injury had been merely covered with a clean dry dressing arrived in the best condition. In the author's opinion the limit of reduction in gross mortality by the application of therapeutic measures is now being approached; further improvement might be attained by propaganda posters demonstrating such accidents and their appropriate first-aid treatment and by the institution of home visiting by trained social workers in order to supervise after-treatment and to give advice on the prevention of further accidents.

Use of *ctab*.—Colebrook, Gibson and Todd describe experimental and clinical work on first aid to burns and scalds. In very severe burns the preservation of life transcends other considerations. The administration of morphine (if possible) the maintenance of warmth and immediate transport to hospital are essential. Clothing should not be removed and blankets, usually septic, must not touch the burn. In lesser, accessible burns of the limbs and head the prevention of infection, especially by haemolytic streptococci, takes precedence. If speedy transport of the patient to hospital or to a practitioner is possible, the burn should simply be protected by a clean towel or sterile cloth, such as should be kept stored in tins in establishments in which burns often occur. Major burns (if the transport of the patient to hospital is unavoidably delayed) and minor burns suited to home treatment, with the surrounding skin, should be smeared with cetavlon (cetyltrimethylammonium bromide, *ctab*.) ointment by means of a knife or spoon sterilized by boiling. The burn is not washed or the blisters incised. The operator, with hands scrubbed and dried, wears a clean handkerchief tied over mouth and nose. The ointment found experimentally to be the most satisfactory is called at Glasgow Royal Infirmary, where the tests were made, 'Number 9 cream'. It contains cetavlon, sulphanilamide, castor oil, beeswax, wool fat, cetyl alcohol, glycerin and water. The proportions and method of preparation are detailed. A clean towel or lint is bandaged over the ointment. Only in cases for which plenary treatment is unavailable—as on a small ship—should the ointment remain on for more than 2 days, as dermatitis may ensue. Olive oil, flour and coagulant jellies, which are neither cleanly nor easily removed, are inadvisable. Morphine alone relieves severe pain; analgesics in ointment for minor burns are unnecessary in first aid, transient in effect and potentially toxic.

Surface treatment of burns

Review of various substances used.—In a paper on the surface treatment of burns, Clowes, Lund and Levenson compare results of treatment with tannic acid, silver nitrate, triple dye and Vaseline or boric ointment in 150 cases treated at the Boston City Hospital. These included only second and third degree burns caused by a great variety of agents, which occurred in patients of all ages from 4 to 79 years. The tannic acid-silver nitrate treatment was used only on burns of the body, arms and legs; triple dye was used for all parts of the body, including hands and face; ointment dressings were used for hands, face, feet and genitalia, and in some cases as the only treatment for burns of other parts of the body. Seventy-five patients had second degree burns only; in 2 of these slight clinical infections occurred; no patient died. Eighteen patients with 10 per cent area or more of third degree burn all had severe infections, irrespective of the surface treatment used and in spite of adequate sulphadiazine treatment. In 11 of these 20 per cent or more of surface area was involved; only 3 patients survived. Although there is no conclusive evidence of the superiority of one type of treatment over the others, the statistics suggest that tannic acid-silver nitrate is least safe for large third degree burns. It was found that areas treated with Vaseline gauze could be grafted earlier than those treated by the other two methods. Skin healing of second degree burns of all areas was later under treatment with tannic acid than when ointment or triple dye was used, whereas second degree burns of the back healed most quickly under Vaseline gauze or boric ointment.

Chemotherapy

Sulphanilamide ointment for severe burns.—Evans and Hoover describe the treatment of severe burns by the application of a primary dressing of sulphanilamide in a fatty base

ointment. The method can be easily adapted to mass casualty use either in civil or in military practice. All the patients treated by the authors had severe burns and were in hospital. The sulphanilamide ointment used was inexpensive and was easily prepared; it was made from equal parts of sterile lanolin and cold cream to which 6 per cent by weight of sterile sulphanilamide powder was added and thoroughly mixed in. The resultant absorption of sulphanilamide into the blood was very slow. Sulphanilamide was used in preference to sulphadiazine because it appeared to cause less unfavourable reactions. Every effort was made to convert contaminated injuries into clean wounds by proper excision of necrotic tissue and by gentle cleansing with white soap and sterile saline. Luminal-sodium with morphine was used for anaesthesia. After preliminary cleansing a liberal quantity of the oil-base ointment was applied to all burned areas, and sterile surgical compresses were placed over the ointment. Then a pressure dressing was applied, except in facial burns, and the patient was put to bed lying on sterile sheets. When the limbs were involved splints were used. If a burn was seen late or was infected when first seen warm continuous saline compresses were used on the burned areas until they were surgically clean. Sulphathiazole was given by mouth and sulphanilamide powder was applied locally to the infected lesions. Administration of plasma was used to combat shock. Every person attending the patient wore a mask in order to reduce the risk of mouth-borne infection by haemolytic streptococci. The primary dressings were left in place for from 7 to 9 days in order to permit the processes of natural repair to go on. The authors report that the results were excellent and that the mortality rate was low.

Drugs in common use

Effects on rats' muscles.—Baker describes experiments made on rats for the purpose of studying the local necrotizing action on normal muscle and the generalized effect after absorption of various detergent and therapeutic agents in common use on large burns and wounds in human beings. The substances tested were applied to the exposed abdominal muscles of rats. The local action was determined by counting the number of necrotic muscle fibre layers 24 or 48 hours after application and the general action by observing the rats' behaviour during this period and by histological examination of the main viscera after necropsy. Isotonic sodium chloride, boric acid ointment and motor oil were used as control substances because they have no necrotizing effect. All the detergent substances used had some such effect. White soap, ether and benzene caused necrosis of the superficial fibre layers; hexylresorcinol, 50 per cent hydrogen peroxide, 50 per cent aqueous medicinal soft soap and 95 per cent alcohol caused necrosis of 2–3·5 fibre layers. Absorption of benzene, of 50 per cent hydrogen peroxide and of 95 per cent alcohol caused death. Baker suggests that if cleansing of a burn requires a substance other than isotonic sodium chloride, white soap should be used. Its effect is not less necrotizing than that of ether or benzene but it has neither the inflammability of the one nor the toxic effect of the other. Three escharotic solutions were tested, tannic acid, tannic acid-silver nitrate mixture and triple dye. Concentrations of 10, 15 and 20 per cent tannic acid were used in the mixture, the silver nitrate concentration being kept at 10 per cent. The local necrotizing action affected 8–9 fibre layers with all the solutions and did not vary with the concentrations of tannic acid. Hepatic damage occurred in those cases which were treated with tannic acid alone and with the silver nitrate mixture containing 20 per cent tannic acid. Triple dye caused the death of 7 out of 10 rats which were tested but no visceral changes were found to account for this.

Superiority of viacutan over tannic acid

The ideal medicament for burns must penetrate epithelium, form a resistant flexible coagulum conservative of fluid, be scorchingly bactericidal and provide a solution of low surface tension for percolation into the folds of the skin. Pick and Barton find these desiderata in silver dinaphthylmethane disulphonate employed in 1 per cent solution as viacutan. Its bactericidal activity is 20 times greater than that of phenol. Free addition of horse serum to the broth magnifies its bacteriostatic activity to *Staphylococcus aureus*. Experimentally, viacutan equally with tannic acid rendered tissues resistant to lysis by proteolytic enzymes and its penetration was 10 times speedier than that of tannic acid. The presence of silver in the blood stream or in any organ was not traced. Of 80 cases treated 7 are cited as representative of out-patient treatment and 10 as illustrative of in-patient treatment. In the case of out-patients viacutan was applied to the burn on one layer of gauze and when the gauze had dried a bandage was put on. The gauze, which was usually removable within 48 hours without disturbance of the coagulum, was allowed to remain when it was adherent. When parallel areas were treated with viacutan and with tannafax or with triple dye, viacutan proved to be speedier in action. In the case of in-patients routine administration of morphine with application of heat and giving of fluids sufficiently deadened the pain associated with the dressing of lesser burns but anaesthetics were given when extensive burns were dressed. After cleansing with normal saline and excision of blisters had been carried out, the burn and a margin of skin was painted with viacutan; the painting was repeated within 12 hours. The use of an electric hair-dryer or powdering with zinc oxide and starch or sulphanilamide accelerated drying. The coagulum separated in from 8 to 12 days. Sterile pus, sometimes occurring, did not entail inflammation or delay healing. Skin-grafting was unnecessary. Pain was rapidly relieved. Although face and hands were often involved scarring was slight and mobility was free. The period of disability was curtailed.

Sealing of capillaries

Use of human fibrin.—Because various coagulants that were tried failed to stem the exudation from burned surfaces Macfarlane considers that the capillary walls are responsible for the loss of fluid, especially as blister fluid clots normally in a test-tube. Mechanical sealing is necessary and human fibrin seemed physiologically ideal for the purpose of trial. Production in situ of a tough adherent membrane by means of fibrinogen solution or dried fibrinogen clotted by spraying with thrombin, failed to stop the exudation. Therefore a fibrin membrane was prepared by mixing 450 cubic centimetres of plasma with 100 cubic centimetres of 1·18 per cent calcium chloride and 0·05 cubic centimetre of 1 in 100,000 Russell's viper venom. The mixture was poured into shallow dishes and allowed to clot. After being washed, the membranous clot was dried between sheets of blotting paper. Sterilization of the membranes, suspended in saline, was effected against non-sporing organisms by heating them to 80° C. for a period of one hour or to 70° C. for a period of 2 hours. The membranes appeared to keep indefinitely; dry preservation caused unworkable fragility but elasticity was restored when they were soaked in water; disintegration occurred after the membranes had been immersed in saline for 3 weeks. Burns in 8 patients and 2 experimental burns on the investigators' forearms were treated by gluing the membrane to the cleansed burned surface with fresh fibrin. The method, although practicable, is without therapeutic or economic advantages over accepted methods. Pain is rapidly relieved and the dressings are comfortable but not more so than is the case with many other treatments. Rapid lysis dissolves the membrane in infected cases. The problem of fluid loss persists. A postscript reports encouraging results from employment of fibrin membrane soaked in thrombin as a haemostatic in haemophilia and, at Harvard, fibrin membranes mollified by glycerol have given satisfaction in the treatment of burns.

Experiments with closed-plaster methods.—Glenn, Gilbert and Drinker declare increased capillary permeability to be the obstacle to the successful treatment of burns and to successful healing. Vasodilatation renders a large burn comparable to a suddenly opened reservoir, the walls of which are also leaking, into which the blood flows; one-third of the total blood volume may be lost. Slow intravenous infusion of plasma is the rational treatment since rapid introduction promotes further extravasation. Excess of coagulated plasma forms a nidus for bacterial growth and its fibrous organization induces deformity. The closed-plaster method aims at limitation of exudate by holding the part, without pressure, to the same volume as when the plaster is applied. Experiment was first directed to ensure satisfactory circulation under the plaster cast. The paw of an anaesthetized dog was subjected to a standardized burn and in a metal container was immersed in plaster 3 centimetres beyond the burn. When the plaster was set studies were pursued and the lymph was collected by cannulation of a lymphatic vessel above the plaster. Circulation continued satisfactorily. A second set of experiments for the purpose of testing the curative efficiency of this method was made by using the same procedure or by investing the burned part with plaster bandages over sterile gauze. It was found to be essential to invest the parts distal to the burn. Healing without deformity was unusually rapid when capillary leakage was thus restrained. Freedom from pain was noteworthy but whether or not this feature of the treatment will be equally so in the case of human beings has still to be confirmed by clinical observation. When the results of animal experiment are applied to clinical practice the necessary delay in investment in plaster must be remembered. In treating burns in man the dusting of the burn with sulphonamides is suggested in order to make allowance for the insusceptibility of the dog to bacterial and especially to streptococcal infection.

Effect of liver extracts

Prinzmetal, Hechter, Margoles and Feigen present evidence that the liver contains a principle the activity of which significantly decreases mortality from shock due to burns in rats and in mice. The principle exists in extracts which are prepared to contain the anti-anaemia principle but its activity is distinct from that of the anti-anaemia principle. The evolution of a method for producing scalds of standard degree is described. The procedure entails total immersion, head and neck excepted, of the anaesthetized animals in a water bath thermostatically controlled at 60° C., for 15 minutes with specified variations. A time-mortality curve for the control groups of animals was prepared for comparison with the corresponding curve of those subjected to intraperitoneal injection of the extract before immersion. This comparison assesses the activity of the various preparations tested. Rosenthal describes a similar procedure. Experiments with 3 commercial anti-anaemic extracts showed immense increase in survival time. One extract was selected for extensive tests which confirmed the consistent activity of liver against burn shock. Next, liver extracts prepared by Subbarow, highly purified yet containing amounts of anti-anaemic principle equivalent to the cruder extract, were found to be inactive against burn shock; this fact proved that the two principles are distinct. So far steps towards isolation of the principle indicate that it is thermostable and survives high temperature aeration. In water it is soluble and precipitated by acetone and ethanol (ethyl alcohol). Subject to further experiment it is believed to be ineffective after the onset of shock. Solution of sodium chloride 0·09 per cent administered in large amounts is effective against burn shock but its effect is much reinforced by the giving of liver extract.

Maintenance of protein nutrition

Result of investigation of nitrogen metabolism.—The problem of maintaining protein nutrition

in the patient with severe thermal burns is discussed by Taylor, Levenson, Davidson and Adams, who have studied the nitrogen metabolism in a series of cases. The following abnormalities were observed. (1) Azotaemia of two types, reversible and irreversible. The former was associated with transient oliguria and was a common early complication. Restoration of a normal urinary output resulted in the return of the non-protein nitrogen content of the blood to normal. In irreversible azotaemia oliguria was present early but the urinary output was soon restored to the normal; notwithstanding this azotaemia persisted and the patients ultimately died. Kidney function was not sufficiently damaged to account for so much nitrogen retention and it is suggested that increased protein katabolism is an important factor in its production. (2) Increased residual (undetermined) nitrogen in the blood and urine, probably reflecting the presence of abnormal protein metabolites. (3) Hypoproteinaemia, which occurred in half the number of patients. It was associated with increased loss of nitrogen in the urine and tended to be progressive. According to the authors, hypoproteinaemia probably results from destruction of structural protein and may be toxic in origin. In order to restore the nitrogen balance forced feeding with protein products, for example intravenous administration of amino-acids, may be necessary.

External pressure

Experiments on guinea-pigs.—External pressure has been advocated as a method of treatment for burns. It may be applied in the form of tight plasters or as pressure dressings and acts by reducing local oedema and therefore also plasma loss. Rossiter has carried out experiments on guinea-pigs in an attempt to prevent the rapid accumulation of oedema fluid in the skin after burning. The guinea-pigs were anaesthetized with nembutal (pentobarbitone soluble) and burns were made over the flanks. The legs were placed in a glass vessel covered by a rubber cuff such as is used in measuring blood pressure and controlled air-pressure was applied to the burned area. It was found that external pressures of about 10 millimetres of mercury greatly reduced the occurrence of oedema in the burned skin. The pressure was most effective when applied immediately after the burning but was still beneficial if applied 3 hours later. It is suggested that if burns of the human body are treated thus the pressure should be applied early and should be maintained for about 48 hours. The development of oedema was not affected by the application of (1) tannic acid 20 per cent, (2) tannic acid 10 per cent and silver nitrate 5 per cent, (3) gentian violet 2 per cent or (4) triple dye. In burns in human beings, however, coagulating agents may be of use in preventing the external loss of fluid from exposed surfaces. In an appended note Peters points out that it is not yet determined whether or not the reversal of oedema shortens the healing time in burns but that the experiments indicate that pressure may be of value in first-aid treatment.

General principles reviewed

The aim in treating burns, according to Franklin, is three-fold: (1) to preserve life by controlling shock, (2) to anticipate infection and (3) to minimize deformity. Concentration on counteracting pain by administration of morphine and of lost fluid by the giving of plasma infusion must not cause the importance of food and drink to be overlooked. Overheating of the patient must be guarded against. The tanning method entails first an elaborate cleansing, which sometimes may take 3 hours to effect, rather than a cleansing by speedier methods under general anaesthesia. When the first injection of morphine begins to lose its effect an intravenous injection of $\frac{1}{4}$ grain should be given. Six sprayings of 2.5 per cent tannic acid can be applied within 45 minutes if an electric hair dryer is used for each coat. Tannic acid is unsuitable for use over joints, near the lips and eyelids and where hair is abundant. Gentian violet and triple dye are extensions of the tanning principle, the antiseptic value of which does not do away with the necessity for thorough cleansing. Saline compresses and baths with early skin grafting are ideal as treatment for burns of the true skin in which resultant deformity is always a danger to be avoided. Replacement of lost serum, application of pressure in order to minimize further loss, and skilled nursing are here vitally important. The use of the irrigation envelope, preferably the Bunyan-Stannard bag, is outstandingly successful in burns of the extremities. The bag should be partially filled with a 5 per cent solution of sodium hypochlorite and the irrigations given thrice daily for 20 minutes. Between irrigations partial inflation of the bag with oxygen will dry the limb. After healing, which occurs in about 3 weeks' time, the epithelialized surface should be anointed night and morning with lanolin. Physiological saline solution and air suffice when sodium hypochlorite and oxygen are unobtainable. After meticulous cleansing, insufflations of dry sulphanilamide powder covered with tulle gras, or less desirably Vaseline gauze, constitute a method of wide application. The dressing under a firm crepe bandage should remain undisturbed for 3 weeks unless discomfort necessitates redressing. First-aid treatment is useful only in very minor burns.

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CANCER

See also B.E.M.P., Vol. II, p. 737; Interim Supplement, No 10*; and Cumulative Supplement, Key No. 212.

Pathology and aetiology*Experimentally produced cancer*

Administration of oestrogen to male mice.—Bonser describes the effect of administration of oestrogen on male mice of 2 familial strains not previously tested. The effect of castration associated with oestrogen administration on male mice of Strong A strain was also studied, and the effect of foster-nursing on the incidence of mammary and testicular tumours in oestrogen-treated male mice of tested strains was noted. In 10 strains of male mice previously tested with oestrogen, 4 strains proved to be susceptible to the development of interstitial-celled tumours, whereas 6 strains were generally resistant. In the author's strains (IFS and 'white label') the incidence of mammary tumours after oestrogen administration was not noticeably higher than it was among breeding females. The milk factor did not appear to play any part in the genesis of testicular tumours, since foster-nursing by resistant or susceptible females did not preclude or induce their development. Foster-nursing by susceptible female strains led, however, to a high incidence of mammary cancer among susceptible males, whereas in males suckled by resistant strains of females mammary growths rarely developed. Castration appeared to cause only a very insignificant increase in the incidence of mammary cancer in susceptible males; factors other than the absence of circulating androgens were probably concerned. An interstitial-celled carcinoma was successfully grafted from a female Strong A mouse into another female of the same strain; this shows that such tumours are transplantable. Such grafting in successive generations of normal females and oestrogen-treated males indicates that the tumours are dependent upon the presence of oestrogen for continued growth.

Hypoproteinaemia

Ariel, Abels, Pack and Rhoads have observed that in patients with gastro-intestinal cancer a negative nitrogen balance after operation is prone to develop, and suggest that this is due to deficiency of stored protein in the tissues. They have studied three groups of patients. Group (1) consisted of 47 with gastro-intestinal cancer who were submitted to operation; group (2) of 9 with non-neoplastic disease of the gastro-intestinal tract; group (3) of 9 women operated upon for gynaecological complaints. The pre-operative concentration of serum protein in group (1) averaged 6.31 grammes; in 21 patients it was below normal limits. During the first 5 days after operation the concentration fell in 40 patients by an average of 0.81, and 41 were found to be hypoproteinaemic. In group (2) the serum protein averaged 6.54 grammes per cent. Three patients showed hypoproteinaemia. After operation a fall in serum protein averaging 0.18 gramme per cent occurred in 6 patients and 4 were found to be hypoproteinaemic. In group (3) the pre-operative concentration averaged 6.61 grammes per cent. Four were below the normal limit. A post-operative fall averaging 0.38 gramme occurred in 5 patients. The excretion of nitrogen was approximately equal in all groups.

Treatment*Plastic surgery*

Its use in superficial malignant disease.—Pickerill draws attention to the great use of plastic surgery in the treatment of superficial malignant disease. The surgeon who treats such cases may consider that wide and early excision of the growth is desirable but he may be deterred by the difficulties of filling the resultant tissue gap, forgetting the potentialities of modern plastic surgery. He points out that such excisions may be inevitable in some cases, as when a growth has become radio-resistant or when irradiation necrosis has resulted. He stresses the necessity for wide excision in malignant growths of the scalp and melanoma suspected of malignancy. Again, in recurrences of the growth after mastectomy, wide excision would appear to offer the patient the best chances of survival. In such cases Pickerill considers it the primary duty of the surgeon to excise the growth widely and freely with the object of complete eradication of the growth, leaving the tissue gap to be filled by plastic surgery. He believes it to be advantageous if the excision and restoration are done by different surgeons, so that the surgeon who excises the growth is not subconsciously influenced by the future difficulties of tissue restoration. In one case which he describes in order to illustrate methods of restoration, a hiatus in the lip after radium therapy was repaired by means of a tube graft from the neck,

and the writer uses this case to illustrate his belief that radiologists should so arrange their dosage that complete eradication of the growth is ensured even although this may result in tissue necrosis. He believes that a tissue hiatus after irradiation therapy is better than either an extending or a radio-resistant growth, for as he has shown, the tissue loss can be satisfactorily repaired by plastic surgery.

Ariel, I. M., Abels, J. C., Pack, G. T., and Rhoads, C. P. (1943) *Surg. Gynec. Obstet.*, **77**, 16.

Bonser, Georgiana M. (1944) *J. Path. Bact.*, **56**, 15.

Pickerill, H. P. (1944) *Aust. N.Z. J. Surg.*, **13**, 147.

CATARACT

See also B.E.M.P., Vol. III, p. 1; and Cumulative Supplement, Key No. 216.

Acquired cataract

Symptomatic cataract

Experiments in anoxia on rats.—Bellows and Nelson discuss the question of the production of cataract as a result of anoxia and give some details of an experimental investigation. The authors point out that the transparency of the crystalline lens is dependent upon the proper utilization of the nutrient material supplied by the aqueous and that in the event of local deficiency of a vital constituent the lens becomes opaque. The observations of other workers show that deprivation of cystine results in cataract in the larvae of the salamander and it is known that deficiency of riboflavin leads to cataract in rats. Bellows and Nelson emphasize that the most vital requirement of tissues is an adequate supply of oxygen; the rapid replenishment of oxygen in the aqueous is made possible by a diffusion of oxygen from the ciliary body and also from the atmosphere through the cornea. Any shortage of such supply has an adverse effect upon the lens. In the experiments rats were placed in a steel decompression chamber in which the pressure was gradually reduced until it became the equivalent of that at an altitude of 30,000 feet. Fifty per cent of the rats died and about 75 per cent of them and 10 per cent of those still living showed opacities of the lens. Control experiments allowing for the constant flow of 5 per cent oxygen and 95 per cent nitrogen were also carried out; opacities of the lens were again noted but in lesser degree. The authors consider that their experiment showed that cataract can develop during anoxia and that pressure and asphyxia are not important factors in this connexion.

Review of associated disturbances.—Buschke classifies cataract into three groups: diabetic, tetanic and dystrophic. (1) The diabetic group includes lactose and galactose cataract in rats, rabbits and mice, and xylose cataract in rats. (2) The tetanic series is seen in progressive hypoparathyroidism and idiopathic tetany, in parathyroidectomized animals and in dietary tetanic cataract in rats and rabbits. The cataracts found in Gee-Herter disease (coeliac disease) and in osteomalacia probably belong to the tetanic group. (3) The dystrophic group Buschke explains on the basis of a hereditary primary metabolic disturbance in the affected tissues. Riboflavin deficiency, chronic thallium poisoning and tryptophan deficiency have produced cataracts in rodents. Clinical cataract syndromes associated predominantly with atrophic dermatoses are seen in the Rothmund and the Werner syndromes. In the former the cataract develops between the second and the sixth year of life and becomes mature within a few days or months; associated with the accompanying skin disease (poikiloderma vasculare atrophicum) is atrophy of the gonads. The cataract in Werner's syndrome appears in the third or fourth decade; scleroderma, changes in the hair, endocrine manifestations and keratitis bullosa are other features. Cataract may co-exist with atopic dermatitis; in Andogsky's syndrome the lens changes commence in the second or third decade and there is associated a superficial keratitis with manifestations of hypersensitiveness. Cataract associated with keratosis follicularis, telangiectasis and myxoedema have also been described. Cataract may also be found in mongolism. Many forms of the condition remain which are unclassifiable. The most unifying feature of the dystrophic cataracts is the association with lesions of the cornea, skin and testes; in contrast, disease which involves chiefly the haemopoietic or central nervous system is not generally complicated by cataract.

Treatment

Sulphadiazine administered as a prophylactic in extraction cases.—In a series of 312 cases Guyton and Woods have studied the results of the oral administration of sulphadiazine as a prophylactic measure in cataract extraction. The incidence of infection was compared with two control series of 159 extractions and 642 extractions respectively. In the first control group the technique of treatment was exactly similar to that used in the test cases but in the second group both the pre-operative preparation and the operative procedure varied. In the test cases and in the first control group corneoscleral and conjunctival sutures were used; in the second and larger control group either sutures were not used at all or conjunctival sutures only were inserted. In each of the 3 groups the first eye dressings were carried out between the first and fourth post-operative days and the eye was then irrigated with argyrol (mild silver proteinate) and boric acid solution once daily. Each patient in the test series received 3 grammes of sulphadiazine the night before the operation was to be performed and 1 gramme 3 times daily for 7 days afterwards unless toxic reactions were noted; they occurred in 24 cases. Sulphadiazine was not given to patients with albuminuria or with impaired renal

function. The blood concentrations of sulphadiazine were estimated on the second and fourth days during administration; leucocyte counts were also made. In the test group of patients who were given sulphadiazine the incidence of all types of post-operative inflammatory reaction, both questionable and apparent, was 1.6 per cent, as compared with 7.5 per cent and 9.7 per cent respectively in the first and second control groups. There are 3 disadvantages in the use of sulphadiazine prophylaxis: (1) the patient may become sensitized and thereafter may not be able to take any of the sulphonamides; (2) sulphonamide administration increases the amount of post-operative attendance and care which is required; (3) the cost per head of oral sulphadiazine prophylaxis is considerable. The satisfactory results obtained however appear to outweigh the disadvantages. The local use of sulphadiazine powder appeared to cause irritation in a group of 20 cases and is not considered to be justifiable.

Technique of extraction.—The ophthalmic ward of a hospital is the ideal environment, according to Butler, for the patient's mental comfort and for operative success in cataract extraction. Butler prefers preliminary iridectomy not only because he considers it to be the safest method but also because it gives the operator an indication of the patient's behaviour at extraction and because, as the coloboma allows estimation of the size of the lens to be estimated, the surgeon is able to concentrate solely on the section. A few days should elapse after irrigation of the lacrimal sacs. The only general treatment necessary is to have the bowels thoroughly emptied; purgatives should not be given but an enema may be, if required. Butler found that about 4 instillations of 2 per cent cocaine with eserine, a few drops given every 5 minutes, were sufficient for the purpose of local anaesthetization. The iris hook is to be preferred to forceps except when the operator is a novice. Ophthalmic scissors should be held with the thumb and ring finger engaging the loops of the handles, the index finger resting on the hinge and the middle finger resting below the ring finger loop. Extraction was carried out a month after iridectomy. Novocain and adrenaline injected into both cyclids and into the temple half an hour before operation made akinesis certain. Too lavish instillation of cocaine is to be deprecated and general anaesthesia is to be avoided because it may induce post-operative vomiting. In Butler's operations a nurse held the patient's hand centrally across the chest and the direction given to the patient was, 'Look at your hand', not 'Look down'. The patient kept the mouth open during operation so that he could not easily tightly close the eyes. Smith's knife was the instrument preferred. Delivery of the lens was by traction not by expression. Difficulties might arise from non-rupture of the capsule, from too small a section or from a shrunken vitreous necessitating removal of the lens by the vectis. In double cataract in an elderly patient, after attaining success in one eye the second should be left undisturbed because, added to the risk of failure, there is the risk of physical and mental degeneration. Young and healthy patients must decide for themselves without urging from the surgeon. In unilateral cataract good vision in one eye contra-indicates operation in the other. The risk from hypermaturity is negligible.

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Buschke, W. (1943) *Arch. Ophthalm., N.Y.*, **30**, 751.

Butler, T. H. (1943) *Brit. J. Ophthalm.*, **27**, 495.

Guyton, J. S., and Woods, A. C. (1943) *Amer. J. Ophthalm.*, **26**, 1278.

CEREBROSPINAL FEVER

See also B.E.M.P., Vol. III, p. 39; and Cumulative Supplement, Key No. 223.

Clinical picture

The ordinary form

Classification of different types.—Adams points out that an infection due to the meningococcus is in reality a systemic and not, as hitherto described, simply a localized disease, and that acute cerebrospinal meningitis is therefore merely one of the manifestations of a bacteraemia. Non-meningitic forms of the disease occur which, if they remain unrecognized, may eventually lead to serious consequences. The reasons for the sporadic nature of the infection are as yet imperfectly understood but varying degrees of susceptibility in the individual and in the virulence of the organism are probably important factors. A large proportion of patients complain initially of upper respiratory symptoms of some kind, irrespective of the form which the disease will take ultimately; the author makes a classification under four headings. (1) The classical acute cerebrospinal meningitis type, in which delirium, stiffness of the neck muscles and usually a rash are the prominent features; (2) the acute fulminating septicaemic variety, in which there is a sudden onset, profuse skin eruption and extreme prostration, followed by death before treatment can avail; (3) a less severe form in which inflammation of the joints and aching in the muscles of the extremities are the main characteristics; (4) a chronic type in which febrile attacks, with joint pains and a mild eruption, occur periodically. Fluid from a lumbar puncture will be normal in all except the first group. Sulphadiazine, the sulphonamide drug of choice, given early and in large doses, is an almost certain cure except in the acute fulminating type, when adrenal cortical extract may be useful in combating collapse. The first dose of sulphadiazine should be given intravenously and supplemented by antimeningococcal serum in all severely ill patients.

Complications and sequelae*Thrombosis of artery*

Gangrene of right arm.—Levin and McElroy describe a case of cerebrospinal fever with thrombosis of the right axillary artery. Gangrene of the right arm ensued and amputation became necessary. The patient was a colonel, 47 years of age. He had had malaise for one week and was admitted into hospital semicomatose and febrile, with petechiae over the trunk and limbs and small ecchymoses on the upper limbs. There was not any splenomegaly. Kernig's sign was positive. The cerebrospinal fluid was thick, purulent and blood-stained and on culture gave a good growth of meningococci. There were 30,000 leucocytes per cubic millimetre of blood with 93 per cent neutrophils. Meningococci were found on blood culture. The patient could not take fluids by mouth, so intravenous glucose-saline was given by drip method. During the first 12 hours, 5 grammes of sodium sulphapyridine were given in the drip fluid and 2 grammes were given directly into the right antecubital vein. Two intramuscular injections of 2 grammes each were then given every 4 hours. There was not any improvement, so the drug was changed on the third day to sodium sulphadiazine. Four intravenous injections totalling 12 grammes were given and then the drug was continued orally until 51 grammes of sulphadiazine had been given over 16 days. Some 24 hours after admission the patient's right arm was found to be immobile and cold. The radial and brachial pulses were impalpable, but some pulsation was felt high in the axilla. Three days after admission a line of demarcation was seen 2 inches above the elbow. Next day he regained consciousness, and from then on his general condition improved rapidly, but the right arm was becoming gangrenous. Amputation had later to be done, leaving 2½ inches of the upper humerus. Progress was good apart from a small pulmonary infarction 5 days after operation. Microscopical examination showed thrombosis of the right axillary artery. The authors suggest that meningococcal emboli impaired the blood supply to the axillary artery and that this resulted in damage to its walls and in thrombosis.

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CHILD HEALTH AND WELFARE

See also B.E.M.P., Vol. III, p. 132.

Growth and development*General discussion*

Effect of war conditions.—Milligan discusses the subject of children's health and nutrition during the war, with particular reference to his own administrative area in Derbyshire. When records of the growth, strength, and endurance of schoolboys were compared in June and in September 1941 with those of January and February 1941, a serious deterioration was found to have taken place. The most likely operative cause appeared to be lack of first-class protein. The arrival of foodstuffs in large quantities from the United States of America completely changed the picture and by the end of 1943 the pre-war level was being reached. Some 35 per cent of 200 boys investigated were deficient in vitamin C and these children were more liable to fatigue and infection than were 200 controls who had been receiving multiple vitamin capsules. About 16 per cent were certainly deficient in vitamin A and these suffered more than did the controls from acne, skin sepsis, chilblains, and bronchitis. With regard to infants, mortality rates during the war had not altered much from those of pre-war years. With regard to infant growth, males in the war period in the early weeks of life weighed less and measured less than did those in the pre-war period, but the average rate of growth of male infants during 1940-2 was faster than was the pre-war rate, so that at the end of the first year of life the children were heavier and longer than were those in the pre-war group. Female infants, on the other hand, showed no difference during the war in average rate of growth or in weight. The increased rate of gain in weight in males was noted after special allowances to expectant and nursing mothers and to children had been put into operation. Nearly 4 per cent of about 1,200 evacuated children suffered from enuresis. In 1939, 12 per cent of evacuees were infested with head lice, but in 1940 the percentage fell to 3.6. Using the Board of Education standard of nutritional state, 10.2 per cent of 224 evacuees were slightly malnourished and 4 per cent severely malnourished. The incidence of minor ailments among evacuated children was trebled in the war years as compared with pre-war years. There was a considerable incidence among them of bronchial asthma, bronchitis, gastric troubles, and injuries. There was an increased incidence of scabies from 1940-2 both in the evacuated and in the Derbyshire children, but there was a decreasing incidence in 1943. Milligan concludes that children as a whole have fared at least as well in war-time as in peace-time, thanks to the measures taken by the Ministries of Food and of Health.

Body conformation in the child

Significance of body creases.—Nassau discusses the significance of (1) the big creases of the body of the infant, (2) the creases of the elbow, and (3) the big flexor creases of the palm. The big creases are most striking on the thighs of the young child, but there are some shallower creases about knees and ankles, and some in the upper limbs and trunk. The creases of the right and left half of the body are asymmetrical. At the end of the first year or in the course of the second year these creases disappear. The opinion has prevailed that the development

of the sense of equilibrium and especially changes in coordination and tone of the muscles are connected with the disappearance of the folds. The connective and elastic tissue of the skin may mature only slowly under the stimulus of functional need. An external expression of this maturing process may be the disappearance of the creases. The creases persisted in one child with congenital myotonia and in another after encephalitis. There is a striking sex difference in the folds of the elbow at the beginning of the fourth decade. In men there here occur no creases or only a slight one, but in women cross folds appear which increase in number and intensity with increasing years. The pattern of the lines of the palm is well known. In a child with mongolism, in place of the usual 3 large lines, 2 are found. An abnormal pattern of the lines of the palm accompanying congenital disease probably indicates an intra-uterine disturbance of development, but a normal pattern with congenital disease suggests a defect in parental germ cells. The pattern in the hand, however, is not changed by diseases which occur in the child after the sixth month of pregnancy. Usually any changes are more marked in the left hand; sometimes they are to be found exclusively in the left hand.

Dentition

Importance of fluorine intake.—It has been recently discovered that fluorine in trace quantities in drinking water is effective in preventing dental caries in children and young adults although large quantities may produce endemic dental fluorosis—mottled enamel. McClure discusses the question with regard to food and water requirements of children of from 1 to 12 years of age. It cannot be said that dental caries is a fluorine deficiency disease, but it has been found that the dental tissues are extremely sensitive to fluorine during the first 7 or 8 years of life, and its addition to children's diets during these years promises to reduce greatly the prevalence of dental caries. It has been estimated that fluorine in drinking-water in quantity of one part per million, plus trace amounts in various foods, gives approximately from 0.5 to 1 milligram fluorine intake daily. This amount is considered to be effective in the health of children of from 1 to 7 or 8 years of age, the important years for tooth formation. It is suggested that fluorine in correct amounts should be added to children's diets or to the water supply in districts in which the latter is either fluorine free or contains suboptimal amounts.

The care and management of normal infants and children

The management of a normal child during early infancy

Dermatological conditions.—During the first month of life infections produce the most serious dermatological conditions, according to Henderson. Urticaria and sweat rashes and napkin rashes are common; scabies and birth-marks are not rare. (1) The *Staphylococcus aureus* is the usual infecting agent, manifested in pustules, onychia, bullous impetigo, boils and abscesses. Prophylaxis of cross infection ranks first. Nurses who harbour any cutaneous or nasal infection should immediately report for relief from duty and infants who display conjunctivitis or other infection must be isolated. Onychia, which affects fingers rather than toes, requires daily application of gentian violet, brilliant green or ammoniated mercury ointment, and the application should include an area of surrounding skin. The infected finger is segregated from neighbouring digits and the hand is gloved in order to prevent contact elsewhere. Infection of the pulp demands adequate surgical drainage, as do boils and abscesses which have not yielded to fomentation. The medicaments mentioned above are appropriate to bullous impetigo and pemphigus, after removal of the raised skin. Gentian violet desiccates the skin after three days; this necessitates the substitution of ichthylol paste. Sulphonamides are doubtfully beneficial in staphylococcal infections, but sulphathiazole (½–1 gramme 4-hourly) may be tried in severe cases. In erysipelas and other streptococcal infections it has revolutionized prognosis. (2) A dusting powder is appropriate to sweat rashes and allergic rashes and, after the flexures have been washed, dried and painted with gentian violet, to intertrigo. Slighter napkin rashes result from napkins which are too rough or are washed inefficiently and with a soap too alkaline, and sore buttocks especially are the result of contact with loose stools. Gauze should be used for the purpose of absorbing the stool; it may be better to dispense with a napkin temporarily; egg albumin may be painted on to form a protective pellicle; a modification of feeding should be the first consideration. (3) Scabies is often detected by its presence in the mother, who must be treated in order to prevent reinfection. Sulphur ointment is effective. The diagnosis of congenital syphilitic rashes depends upon concomitant signs as serological tests are unreliable during the first 3 months of life. (4) The treatment of birth-marks is usually postponed.

Management during late infancy and childhood

Bladder control.—A review of the literature made by Huschka shows that medical knowledge of the age at which training in bladder control should be started is still inadequate. It is of great importance that training should be managed at a time and in a manner which will not produce undesirable emotional reactions and damage to personality. A distinction has moreover to be made between training which is aimed at the production of a conditioned reflex, which is possible quite early in life, and training in voluntary control of micturition, which cannot begin until much later. The author concludes that training of the latter type should not be begun before the age of 10 months, since at an earlier age it is bound to be coercive. She has investigated the history of 215 children who had been referred to a psychiatric clinic. Most of the mothers had at least average, and many more than average, intelligence. Of the 215 children 43 per cent had achieved dryness before the age of 2 years, which the author considers to be too early. In 113 cases data concerning the educative method

employed were available. In 32 (28 per cent) it was coercive and included physical punishment or psychological pressure or both. Of 126 children who had been subjected to such methods or to premature institution of training the emotional reaction was recorded in 94; in 59 of these it had been undesirable. Twenty-four responded by continuing to wet and in most cases anxiety was apparent, either frankly expressed or taking such forms as aggressiveness and compulsiveness. Of 136 cases in which data of functional enuresis were recorded, 79 had a positive history. Fifty of these children had never been able to establish bladder control and in 29 enuresis had developed in connexion with a disturbing emotional situation.

Prevention of neonatal death

Discussion of causes

Main aspects of neonatal mortality.—Asphyxia, birth injury, prematurity and infections are the four main causes of neonatal death considered by Parsons. At birth the adherent alveoli require effort for their aeration and the foetus is physiologically anoxaemic. Exaggerated anoxaemia is either (1) anoxic as a result of maternal respiratory or circulatory disturbance, (2) anaemic as a result of maternal anaemia or erythroblastosis foetalis, (3) stagnant because of obstruction of the cord or because of maternal cardiac failure, or (4) histotoxic as a result of the use of drugs or anaesthetics. As pure oxygen does not promote sustained lung expansion, Barcroft advocates the addition of nitrogen, not of carbon dioxide with which the foetus is already overloaded. When respiratory rhythm is established the giving of carbon dioxide is appropriate. Reduction of fatal asphyxia in the new-born necessitates adequate supervision of the mother during pregnancy, a good obstetric service and an appreciation of the dangers which attend the administration of drugs and anaesthetics. The author is convinced that intracranial haemorrhages are usually catastrophic, and that mental deficiencies and palsies hitherto attributed to haemorrhage have asphyxial origin. If haemorrhagic disease influences the extent and persistence of intracranial haemorrhage, administration of vitamin K to the mother as she is entering labour, or to the infant together with a blood transfusion, should raise the prothrombin level. Increased use of X-ray examination in diagnosis may assist in diminishing the death rate due to intracranial and other birth injuries. A premature child has been defined as one who weighs less than 2,500 grammes even if carried to term. In rearing the premature infant Field's excellent results are attributable to (1) efficient nursing, (2) the use of breast milk and (3) minimum handling of the infant. In Field's cases oxygen and carbon dioxide were administered nasally for recurrent cyanosis. The taking of food should not be forced initially but high caloric value in feeds is desirable later. The liability of the premature baby to haemorrhagic disease as a result of prolonged hypoprothrombinaemia calls for the giving of vitamin K and of vitamins generally. The infections of infancy are often generalized, rapid, feebly resisted and apyrexial. The nasal passages of parent, nurse and doctor may be a source of infection, and the skin, the respiratory and alimentary tracts and the umbilicus are portals of entry. The giving of sulphonamides improves the grave outlook in pneumonia and of sulphaguanidine that in enteritis. The increasing incidence of syphilis should be borne in mind.

The interrelated causes of neonatal mortality Tyson ranks as (1) asphyxia, (2) infection, (3) incorrect feeding, (4) haemorrhage and (5) prematurity. (1) Antenatal care and skilled obstetrics reduce these dangers in general. At present, however, deep analgesia and anaesthesia militate against a reduced asphyxial mortality. Acceleration of the foetal heart or slowing with convulsive activity, during labour, indicates anoxaemia. Oxygen administration to the mother before delivery and as long as the cord pulsates, is beneficial to the infant. Since birth involves some degree of shock, careful handling and warmth are essential; even before severance of the cord, the presence of asphyxia requires clearance of the mouth and pharynx and drainage of mucus by posture or aspiration. Oxygen inhalations (later with carbon dioxide), artificial respiration (preferably by mechanical device) and nikethamide or alpha-lobeline, to stimulate the respiratory centre, come next in order. (2) The prevention of infection depends upon the cleanliness of all nursery staff, especially as regards respiratory infection, and the exclusion of persons not on duty. Thermometer, utensils and clothing, duly sterilized, must be individual to each infant. Milk and its storage demand sterile conditions. The *Staphylococcus aureus* and *Bacillus coli* are especially inimical to infancy. The sulphonamide drugs in pneumonia, erysipelas, and pyelitis are invaluable, as also in septicaemia and diarrhoea, allied in the last with transfusion. (3) Maternal reluctance to nurse must be forestalled by attention to the breasts from the fourth month onward; the nipples should be washed twice daily, proceeding gradually from a soft cloth to a hard brush. A desire to nurse is thus inculcated. (4) Haemorrhagic tendencies are countered by administration of vitamin K to the infant at birth or, if foreseen, to the mother during labour. Grosser haemorrhage requires transfusion, with meticulous cross-matching in erythroblastosis. (5) The prevention of prematurity advances with attention to diet, supplementary vitamins and the control of syphilis. Premature labour requires generous oxygen administration with any concomitant anaesthesia. Continuous attention to detail is required in the subsequent nursing, and this may be lacking if the nursing staff is insufficient and overworked.

Neonatal mortality in America.—The infantile death rate in the United States of America has been halved since 1915 but the neonatal mortality has dropped little, according to Potter. The outstanding causes of the mortality—prematurity, birth injury and infection—are capable of reduction; congenital malformation alone eludes present knowledge. In prematurity the

organs unready to withstand extra-uterine life are the lungs, kidneys and gastro-intestinal tract. Inadequate capillary area leads to anoxia which demands oxygen administration and adequate humidity; breast milk must be available for the feeble digestion. Environment and nursing are therefore vitally important. Decrease in birth injury requires increased obstetric skill, and lessened infection (respiratory, gastro-intestinal, umbilical and cutaneous) clearly depends upon the scrupulosity of attendants concerning hygiene and particularly upon the sterilization of bedding and water. Such minor contributors to mortality as syphilis and haemorrhagic disease are remembered. The Chicago Health Department issued regulations governing the equipment and conduct of delivery rooms and of specially staffed nurseries devoted exclusively to the mother and her offspring. The infants are not dismissed before attaining a weight of 2,500 grammes; their home conditions are inspected meanwhile. An incubator ambulance for transport of babies born at home, and human milk, are available. Such measures have reduced the death rate under one year of age to 40 per cent less in Chicago than in the United States of America generally.

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CLIMACTERIC AND ITS DISORDERS

See also B.E.M.P., Vol. III, p. 228; Interim Supplement, No. 14*; and Cumulative Supplement, Key Nos. 242 and 243.

The climacteric in the female

Clinical picture

Diabetes mellitus and the menopause.—Gitlow and Kurschner point out that the over-activity of the anterior pituitary gland which is associated with the menopause may include increased diabetogenic activity. In the diabetic clinic at Lebanon Hospital, New York, about 90 per cent of the patients are women of menopausal age. Since oestrogen exerts an inhibitory influence upon the anterior pituitary gland it was decided to test its effect upon diabetes in these patients. Thirteen patients were studied; in 8 the onset of diabetes coincided with the menopause; in 2 pre-existing diabetes was aggravated by the menopause; in 3 the menopause occurred long before the onset of diabetes. Two patients who had not any menopausal symptoms and who were allergic to insulin were also treated with oestrogen; it did not have any effect on either of them. The patients in whom diabetes developed at the time of the menopause and those in whom it was aggravated by the menopause all responded favourably to oestrogen. Of those whose diabetes began long after the menopause one was benefited by oestrogen, but in her case evidence of a pituitary tumour was obtained; 2 did not show any response to oestrogen therapy. In all of the patients who were taking insulin the latter was not discontinued but it was found possible to reduce the dose considerably. Three patients were treated by oestrogen and diet alone. Large doses of oestrogen were required; the minimum effective dose was 30,000 international units weekly and most patients needed from 60,000 to 80,000. In only one case was it effective when given by the mouth.

Treatment

Use of ethinyl oestradiol.—Sedative and tonic treatments have failed to abolish the physical and emotional discomforts of the menopause. Oestrogen treatment is more effective. Since stilboestrol is too nauseating for oral use, Lyon advocates the employment of ethinyl oestradiol, the disadvantages of which are negligible. The subjective symptoms of 45 patients during one month's cycle were recorded, with readings of temperature and of vaginal hydrogen ion concentrations and scrutiny of endometrial biopsies. After this controlling procedure, ethinyl oestradiol in daily doses of 0.05 milligram was orally administered over a period of 6 months in 3-week courses separated by intervals of one week. The tablets should be enteric-coated. Abstinence from alcohol is desirable, otherwise the dose may have to be doubled. The study is based on 348 cycles of treatment. Flushes and sweating, which were universal before treatment, were reduced to 2.2 per cent. Insomnia, vertigo and other less common symptoms showed a reduction almost equally satisfactory; depression, palpitation and arthralgia were abolished. After 6 cyclic treatments the medication was withheld for one month in order to assess the results attained. None of the cases had developed hyperplasia of the endometrium. The generally observed diminution of the vaginal pH appeared to be related but not essential to beneficial results. Continuation of the treatment seemed in most cases to be desirable.

Menopausal flushes and vitamin E.—The claim that menopausal flushes are controlled by vitamin E has been investigated by Hain and Sym who, however, have treated only 4 patients in this way. Their results suggest that vitamin E may be of value as an alternative to oestrogen therapy, which possesses several drawbacks, particularly its toxic and possibly carcinogenic properties. The rationale for the employment of vitamin E is obscure, especially as it has been stated to have an anti-oestrogenic action. The preparation of vitamin E used in this study was

viteolin, which is standardized at 6 milligrams of α -tocopherol per capsule. The first patient of the series was aged forty-seven years and had had hysterectomy performed at the age of 45. She started with 2 capsules daily. During the first week the flushes became less numerous but more pronounced; during the second week a reversal took place. During the third week the dose was reduced to one capsule daily. Treatment was continued for 5 more weeks, during which the flushes became greatly reduced in number; in the last 2 weeks of treatment none occurred. The patient then stopped treatment and the flushes recurred, but only at long intervals. A second patient, aged 50 years, with flushes appearing after a natural menopause experienced little or no relief, but probably did not give the treatment sufficient trial. The 2 other patients obtained considerable relief; in one the flushes were reduced from 10 or 15 to 3 or 4 daily. The authors recommend a course of 2 capsules daily for 3 weeks and one daily for the ensuing 2 months.

Gitlow, S., and Kurschner, D. M. (1943) *Arch. intern. Med.*, **72**, 250.

Hain, A. M., and Sym, J. C. B. (1943) *Brit. med. J.*, **2**, 8.

Lyon, R. A. (1944) *Amer. J. Obstet. Gynec.*, **47**, 532.

COELIAC DISEASE

See also B.E.M.P., Vol. III, p. 262; Interim Supplement, No. 18*; and Cumulative Supplement, Key No. 247.

Pathogenesis and aetiology

Infantile type

Association with bronchiectasis.—In 1928 Fanconi distinguished a group of cases of coeliac disease in which symptoms were noticed during the first few months of life, in contrast to the commoner form in which the onset is delayed until the end of the first year or later. Further study of these cases, of which, with Botsztejn, he now reports 43, has shown that the condition is familial in character and is associated with bronchiectasis. The cases may be classified in groups as follows. (1) Newly born infants with ileus and fibrocystic disease of the pancreas, one case. (2) Infants who died within 6 months of birth, 13 cases; in 8 infants gastro-intestinal symptoms predominated, in 5 respiratory symptoms. (3) Children who died between the ages of 6 months and 2 years, 21 cases; gastro-intestinal symptoms were predominant in 7, respiratory symptoms in 14. (4) Children who survived for more than 2 years, 8 cases; in 3, gastro-intestinal symptoms predominated and in 5, respiratory symptoms predominated. In 31 of the 43 cases the condition occurred in a sibling. The cardinal symptoms were: a condition of obstinate malnutrition, dating from shortly after birth; bulky, offensive, fatty stools; chronic paroxysmal cough, resembling whooping-cough; absence of pancreatic ferments from the duodenal contents; a similar condition occurring in siblings. Classical coeliac disease is distinguished from these cases by the presence of pancreatic ferments in the duodenal contents, the later onset and the satisfactory response to treatment. There is some danger of the condition being wrongly diagnosed as whooping-cough. The surviving patients in this series, with one exception, remained thin despite treatment. Treatment of the babies, in open-air conditions, should include proper diet and the administration of pancreatic enzymes. Parents should be warned of the familial character of the disease.

Clinical picture

Five types differentiated

Lapin classifies the type of metabolic diarrhoea known as the 'coeliac syndrome' into five subtypes. (1) Cystic fibrosis of the pancreas—onset at birth. (2) Intolerance of starch—onset between the ages of 3 and 12 months. (3) Infantile steatorrhoea—onset at from one to 8 months. (4) 'Coeliac disease', steatorrhoea—onset at from 10 months to 5 years. (5) 'Allergic coeliac' syndrome. These groups include many patients who have chronic diarrhoea for months or who have frequent episodes of diarrhoea. Most patients with severe coeliac diarrhoea, with or without a family history of allergy, do badly on a diet containing whole cow's milk but tolerate boiled skim milk or protein milk. This intolerance does not prove the presence of an allergy, but may simply indicate inability to digest untreated milk. The importance of routine analysis of stools—not only bacteriological examination but also quantitative chemical analysis for fat and starch—is emphasized. For diagnostic examination the stools are collected for 3 full days with the patient on a normal mixed diet. Under normal conditions the weight of the stools is from 40 to 80 grammes a day according to age, the content of water is 70 to 75 per cent and the content of fat 10 to 25 per cent of the total. Normally there are no free starch granules. The results of examinations of stools are correlated with blood cholesterol values, dextrose tolerance tests and the determinations of duodenal enzymes. Lapin thinks that many more cases of metabolic diarrhoea are seen now than in the previous decade; this may be due to more adequate recognition or to the present vogue for early solid feeds. The fact that the level of amylase in the duodenal contents is low in infants under 3 months old suggests that starch should not be added before that age. The existence of 'allergic coeliac' reactions suggests caution in the routine use of orange juice, cod-liver oil and egg yolk, especially raw, at an early age; the substitution of the non-allergic synthetic substances may be advisable. Administration of the vitamin B complex produces an increase in the duodenal content of lipase. The routine use of this complex might prevent the development

of intolerance to fat. Most infants with metabolic diarrhoeas can tolerate fat better than they can starch; therefore a slight diminution in the fat of milk and the addition of more meat and cheese, but not of cereal, seems to be indicated.

Adult cases

Radiographical findings in idiopathic steatorrhoea.—Brailsford describes the radiographical abnormalities which are manifested in the small intestine and in the skeleton in idiopathic steatorrhoea (alternatively named non-tropical sprue and Gee-Thaysen's disease). Immediately after administration of a watery suspension of barium, radiographs are taken, the patient lying prone. Within 15 minutes most of the jejunum is visible. At first distribution appears to be normal but within 30 minutes the barium masses in curds, small and irregular, or filling isolated and gas-distended segments. In other segments barium lodged in folds of mucous membrane presents a rib-like appearance. Accelerated flow may accompany this disordered tone of the intestine. Within 2 hours barium appears throughout the large intestine and the picture suggests that bulkiness of faeces characteristic of the disease. The initially normal distribution and the later abnormality, persisting although barium passes continuously from the stomach, suggests that some excretion is produced when food enters the duodenum. Possibly this excretion rather than deranged intestinal innervation causes the abnormal pattern. Administration of liver extract and vitamin B complex improves appearances in the small intestine. Radiography may be a guide to treatment. Skeletal defects from disordered metabolism of calcium and fat although sometimes specific may suggest rickets or parathyroid hyperactivity. Specifically, adolescent bones although peripherally defined and smooth do not present a compact cortex. Absence of calcification between the main trabeculae gives them a clearer definition; they appear less packed. The metaphyses of long bones are unusually deep and diaphysal outline is blurred as in rickets. Pliability produces coxa vara and genu valgum. In the hand general decalcification accompanies hypercalcification of the terminal phalanges. The skull shows osteoporosis advancing to general decalcification. Expansion of the intervertebral disks compresses the vertebrae. Physicians concentrate on the alimentary and surgeons on the skeletal disorder but successful treatment requires consideration of both.

Brailsford, J. F. (1943) *Brit. J. Radiol.*, **16**, 283.

Fanconi, G., and Botsztein, A. (1944) *Schweiz. med. Wschr.*, **74**, 85.

Lapin, J. H. (1944) *Amer. J. Dis. Child.*, **67**, 139.

COLDS

See also B.E.M.P., Vol. III, p. 271.

Clinical picture

Effect of sulphadiazine administration

Limited effect.—Cecil, Plummer and Smillie report clinical and bacteriological investigations on 66 members of the staff of the New York Hospital who were suffering from the common cold. Of these, 48 were treated with 3 grammes of sulphadiazine given daily by the mouth for 4 days; the remaining 18 were used as controls. The drug was also given to 6 normal persons and nasopharyngeal cultures were taken from them. This initial study showed remarkable uniformity in the flora of the normal nasopharynx, pronounced reduction in the flora as soon as the blood concentration of the sulphadiazine reached from 4 to 6 milligrams per hundred cubic centimetres of blood, and rapid return to normal after administration of the drug was stopped. The clinical findings in the affected cases were unconvincing. Located cases averaged 8.1 days and controls 9.7 days of illness. Secondary sinusitis or bronchitis did not occur while the drug was being administered, but did occur fairly often after administration was stopped. As a result of the investigation the authors are opposed to the use of sulphonamides in cases of common cold, except in a few cases selected because the patients concerned are already known to be subject to severe secondary infection.

Preventive measures

Vaccines

Report of investigations.—Nowadays especially the loss of working time due to the common cold is much more important than are its minor discomforts. McGee, Andes, Plume and Hinton examine the medical records of five industrial and commercial concerns which had shared in an endeavour to minimize lost time and to determine the effectiveness, if any, of vaccines employed prophylactically. The use in the past of mixed catarrhal vaccines and of the filter-passing virus has been—and remains—discouraging. The efficacy of 2 vaccines for hypodermic administration was tested, namely those of Sharp and Dohme and of Parke, Davis, and also of 3 orally administered vaccines—vacagen, entoral and oravax. Of the two groups of controls one received placebos orally or subcutaneously; the second group consisted of untreated employees who cooperated by reporting the occurrence of colds. The investigation concerned 1,591 individuals. Groups which received the orally administered vaccine, vacagen, the subcutaneous vaccine of Sharp and Dohme or an oral placebo, suffered from the least number of colds, with an average of 0.66 cold per head and an average consequent absence from work of 0.69 day. Groups which received the oral vaccine, oravax, or oral or hypodermic placebos, or which were untreated, suffered from 1.07 colds per head, but with the lesser average of days lost of 0.48 per head. Groups which ingested oravax, or

received a placebo, oral or hypodermic, or were without medication, displayed the mildest infections, which involved an average absenteeism of 0.50 day per cold. The average absenteeism of 1.27 days per cold was recorded in the remaining groups. The geographical area proved to be irrelevant. From differences so minute and inconsistent it only can be inferred that stock vaccines at present available are without value in prophylaxis of the common cold.

Drugs

Patulin and the common cold.—In a series of articles on the use of patulin against the common cold the drug is dealt with from several aspects. Raistrick describes how workers at the London School of Hygiene and Tropical Medicine, who have been engaged for years in studying the moulds, isolated a metabolic product of *penicillin patulum* which was shown to have antibacterial properties and to which the name, patulin, was given. This substance when tested clinically against the common cold has given encouraging results and is still on trial. Birkinshaw, Michael, Bracken and Raistrick describe the methods of cultivating the mould and of isolating and purifying patulin. They suggest a structural formula in accordance with the chemical properties of the compound and describe the various chemical tests which have been applied to it. The results obtained in his own case are reported by Gye who, receiving a sample at a time when he was suffering from a severe cold, tried douching the nasal passages with an aqueous solution of unknown strength. Pain resulted but within an hour the nose was clear; the douching was repeated twice on the same day with a weaker solution. After the third treatment all signs of coryza disappeared. Later the opportunity arose to treat a cold from the beginning. Patulin failed to cure the cold in the early stages but it relieved the nasal stoppage. Thus it appears that patulin has not any effect on virus infections but may completely prevent secondary infection. Of several other volunteers who tried the drug only one failed to obtain relief. Bacteriological investigations carried out by Hopkins showed that *in vitro* patulin possesses bacteriostatic powers against a number of Gram positive and Gram negative aerobic organisms. Preliminary experiments with anaerobes indicate that the drug is active against these also. The addition of pus to the broth medium did not have any inhibitory effect. In a clinical trial 57 per cent of the treated subjects recovered within 48 hours as against 9.4 per cent of the controls. Ill effects were not observed. Patulin in solutions of from 1 in 20,000 to 1 in 5,000 was used; either the nose and throat were sprayed with the solution or the patient was required to sniff it up and to gargle with it. Greenwood adds a statistical note which shows that the difference between the treated and the control groups is most unlikely to have been due to chance.

Use of sodium sulphathiazole and desoxyephedrine hydrochloride

In prevention of complications.—Acute coryza or nasopharyngitis may be caused by a virus or by some of the many varieties of bacteria found in the throat and nose but prolongation of symptoms and complications are caused by pyogenic organisms. Dolowitz, Loch, Haines, Ward and Pickrell discuss the prevention of ear and nasal sinus complications by spraying the nose and throat at the beginning of a common cold with 2.5 per cent sulphadiazine solution in ethanalamines. Observations were made on 103 nurses at the training school in the Johns Hopkins Hospital during the winters of 1942 and 1943. Nurses reporting with colds were placed, without their knowledge, in either a treated or a control group. It was found that the incidence of all complications was noticeably less in the treated group; β -haemolytic streptococcal infections usually cleared up within 24 hours and the virulence of pneumococci and staphylococci was greatly reduced. About 3 per cent of the number of treated patients were sensitive to the sulphadiazine spray, as was shown by sneezing and by increased rhinitis. A generalized cutaneous rash developed in one patient. It is possible that in some patients there may develop a general sensitivity to sulphonamides through their use in a minor ailment and thus their employment in a serious illness at some future time will be unsuitable. Turnbull, Hamilton, Simon and George found that a stabilized aqueous solution of sodium sulphathiazole with *dl*-desoxyephedrine hydrochloride if used early in colds gave great relief; many colds were abated. The presence in the solution of a vasoconstrictor increased the efficacy of the sodium sulphathiazole enabling it to reach the deeper layers of the nasal mucous membrane. The successful treatment of over 1,000 cases of nose, throat and ear infections, complicating the common cold, is described; only 6 unfavourable reactions in patients who were allergic to the sulphonamides are noted.

Birkinshaw, J. H., Michael, S. E., Bracken, A., and Raistrick, H. (1943) *Lancet*, **2**, 625.

Cecil, R. L., Plummer, N., and Smillie, W. G. (1944) *J. Amer. med. Ass.*, **124**, 8.

Dolowitz, D. A., Loch, W. E., Haines, H. L., Ward, A. T., Jun., and Pickrell, K. L. (1943) *J. Amer. med. Ass.*, **123**, 534.

Greenwood, M. (1943) *Lancet*, **2**, 634.

Gye, W. E. (1943) *Lancet*, **2**, 630.

Hopkins, W. A. (1943) *Lancet*, **2**, 631.

McGee, L. C., Andes, J. E., Plume, C. A., and Hinton, S. H. (1944) *J. Amer. med. Ass.*, **124**, 555.

Raistrick, H. (1943) *Lancet*, **2**, 625.

Turnbull, F. M., Hamilton, W. F., Simon, E., and George, M. F., Jun. (1943) *J. Amer. med. Ass.*, **123**, 536.

COLIFORM BACILLUS INFECTIONS

See also B.E.M.P., Vol. III, p. 281.

The genito-urinary tract*Treatment*

Limitations of sulphonamide therapy.—Helmholz compares the bactericidal actions of sulphathiazole and of organic acids in urine containing high concentrations of coliform bacteria. In clinical cases of bacilluria with urinary stasis, diuresis may be ineffective in materially reducing the number of infecting organisms and urinary disinfection by bactericidal drugs may be necessary. From a study of the effects of sulphathiazole on the growth of various strains of *Escherichia coli* (*Bacillus coli communis*) in urine, it appeared that with a strong concentration of organisms the sulphonamide compounds were not bactericidal. This is in striking contrast to the potent action of the sulphonamides on relatively small numbers of bacteria in urine. In urinary infections therefore the bacterial content of the urine must be reduced by diuresis for chemotherapy to be effective, but with urinary stasis the problem may be difficult. Further experiments were therefore carried out in order to determine the bactericidal effects of *p*-oxybutyric acid and of mandelic acid in urine with different conditions of hydrogen-ion concentration and containing varying concentrations of *Es. coli* organisms. It was found that in urine with a reaction of pH 5 a concentration of 0.5 per cent of mandelic acid or of *p*-oxybutyric acid was bactericidal within one or two days. A similar concentration of the above drugs would probably be effective clinically even with urinary stasis, whereas sulphonamide therapy would be unsuccessful.

Helmholz, H. F. (1943) *Proc. Mayo Clin.*, **18**, 481.

COLITIS

See also B.E.M.P., Vol. III, p. 292.

Ulcerative colitis*Clinical picture*

Report of 13 cases of primary sigmoiditis.—Primary sigmoiditis, according to Casper, is not often recognized as a clinical entity in the United States of America. In order to justify itself the term, sigmoiditis, must exclude diverticulitis, lymphogranuloma venereum, tuberculosis, syphilis, pelvic inflammation, neoplasms and reactions due to irradiation. Thirteen cases, comprising 11 females and 2 males, were encountered in 489 examinations by the barium enema method. Pain in the left lower abdominal quadrant is constant, with constipation or diarrhoea and sometimes an alternation of the two. Complaint is often made of dysuria and frequent micturition. Radioscopy is of paramount importance in diagnosis and should be supplemented by radiographs, the diagnostic value of which is increased if the pictures are taken while the barium enema is flowing; the patient should assume supine, oblique and lateral positions. The enema causes discomfort which may frustrate examination unless its flow is frequently interrupted; occasionally some of the contents must be withdrawn by siphon. In the case of patients who are referred to the radiologist with a tentative diagnosis of diverticulitis, suspected cancer or colitis, the results of radiography will exclude the presence of these diseases and of other conditions as well. In the cases which initiated this investigation, especially in the earlier cases, radiography revealed an excessive irritability and spasticity of the sigmoid. The causation of sigmoiditis probably does not differ from that of more generalized colitis although it is believed that not in any of these individuals has more extensive colitis developed. Systemic symptoms were mild and the condition yielded to a low residue diet, hot saline irrigations and the free administration of belladonna.

Casper, S. L. (1943) *Amer. J. Roentgenol.*, **50**, 24.

CONCUSSION AND COMPRESSION

See also B.E.M.P., Vol. III, p. 355; and Cumulative Supplement, Key No. 255.

Concussion*Clinical picture*

Post-concussion syndrome.—Immediate effects of injury to the nervous system tend to improve progressively; later effects tend to increase in severity. Of the latter the post-concussion syndrome is examined by Denny-Brown. The syndrome comprises attacks of headache, dizziness and loss of concentration the onset of which is delayed until the patient first attempts mental and physical exertion. The periodicity coincides with attempted exertion. The headache is throbbing, brief, alternating from side to side and much influenced by posture. Concurrently there is insomnia, depression and emotional instability. Penfield attributes the condition to subdural adhesions but this is probably not correct because headache rarely accompanies subdural scars and when it does it affects only the injured area. Russel's view that the soldier has learned that complaint of headache after a blow on the head may procure discharge does not give satisfaction because the mechanism of this syndrome is rarely one of malingering. Denny-Brown states that the most common causes of the syndrome are: (1) an already existing liability to neurosis so that the injury precipitated the occurrence of a psychoneurotic manifestation; (2) premature return to work; (3) general cerebral damage severe enough to produce mental inadequacy. A history of prolonged unconsciousness differentiates the third from the other 2 causes. Successful treatment depending upon accurate diagnosis has resulted

in the return of 67 per cent of 871 patients to duty. The duration of post-traumatic amnesia is a valuable prognostic guide. According to Symonds's analysis, when memory of current events came back within one hour 77 per cent of the patients were successfully returned to duty but only 52 per cent when the amnesia lasted for more than one week. The resemblance of this syndrome to the so-called effort syndrome necessitates the patient's being engaged in heavy exercise as a test before his discharge from hospital, if relapse is to be avoided.

Theory of concussion

Jefferson reviews the field of clinical and pathological data available on the nature of concussion, and accepts the conclusion that whatever alterations in cerebral blood supply accompany or follow a concussive blow are secondary or epiphenomena, and that the prime cause is a paralytic effect on the neurones of which the brain mass is composed, including those of the brain stem. The location of the area or areas affected in the concussional syndrome is a difficult problem. Jefferson states that there can be little doubt that traumatic stupor is produced by a low-level lesion—hypothalamic and brain-stem. Experimentally it has been shown in rabbits and frogs that if after opening the skull the fourth ventricle is touched with the head of a needle, the animal after showing evidence of pain, falls into a completely comatose state which closely resembles concussion. In man, injuries inflicted on comparable areas, especially in operations on acoustic neuromas, are usually attended, when fatal, by unconsciousness from the moment of operation. A further confirmatory piece of evidence is that neuro-surgical damage in posterior fossa procedures readily results in unconsciousness. Increased intracranial pressure, if of brief duration, does not produce unconsciousness; if the pressure be prolonged consciousness is lost; apparently this is due to a tentorial pressure cone with compression of the diencephalon and the rostral end of the midbrain. The nature of unconsciousness is likened by Jefferson to that of sleep and he prefers to speak of this traumatic sleep as 'parasomnia', a state in which there are no responses to stimuli except those of a reflex nature. Cortical lesions, pure and simple, do not produce parasomnia nor do massive excisions of the cerebral lobes. Lesions in the hypothalamic and brain-stem areas cause hypersomnia and stupor and trauma is considered to produce its effects on consciousness in the same areas. Jefferson then argues that a 'waking centre' must exist within this localization, damage to which results in hypersomnia. The electroencephalographical pattern is often very similar in sleep to that seen after concussion. The activities of the cortex must not be wholly neglected and the longstanding mental confusion, the Korsakov syndromes, the patchy or incoherent memory which persist for many days or even weeks after severe head injuries can be explained only by disturbances of total brain functions. Jefferson states that there is a body of evidence which attests to the production of unconsciousness in a relatively focal manner, and that the focus is not in the cerebral cortex.

Traumatic alteration of cortical cell activity.—Each of three conditions—transient vascular disturbance, physiological neuronal damage and organic cerebral injury—is said to be individually responsible for concussion. Phillips asks if it is justifiable to separate the three because overlapping must occur from case to case and suggests that the term, concussion, should be confined to physiological neuronal damage caused by external violence. There are two implications inherent in the theory of transient vascular disturbance as the sole cause: (1) persisting unconsciousness is not due to concussion alone and (2) concussion *per se* implies complete recovery. The objection to the theory lies in the fact that after a blow on the head a man may remain unconscious until he dies and there may not be any evidence of injury to the central nervous system. The occurrence of conditions implied in the third hypothesis—contusion, petechial haemorrhages and oedema—is not disputed and is often proved by lumbar puncture which under increased pressure discloses blood-stained cerebrospinal fluid. Their invariable presence in concussion is, however, disputed. Evidence pointing to physiological neuronal damage as the cause of concussion has been found in electroencephalograms by Williams, the degree of abnormality in the tracings corresponding to the clinical state of the patient. Littré in 1705 noted the absence at post-mortem examination of visible cerebral lesions in a criminal who, to escape the rack, charged headlong against the wall of his cell. Such observations have frequently been endorsed. Erichsen in 1866 described that variety of unconsciousness which if terminating in death would be expected to show neither macroscopical nor microscopical cerebral lesions, as 'commotio cerebri'. To this condition the term, concussion, should be limited.

Denny-Brown, D. (1943) *Ann. intern. Med.*, **19**, 427.

Jefferson, G. (1944) *Brit. med. J.*, **1**, 1.

Phillips, G. (1943) *Med. J. Aust.*, **2**, 148.

CONJUNCTIVA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 365; and Cumulative Supplement, Key No. 256.

Non-bacterial inflammation

Phlyctenular conjunctivitis

Review of tuberculosis of the eye.—Sorsby describes the manifestations of tuberculosis of the eye. Lesions demonstrating the tubercle bacilli and caseating giant-celled systems occur as a primary affection of the conjunctiva and as metastatic reactions in the uveal tract; choroidal

tubercles may be observed in tuberculous meningitis. Most of the ocular complications of systemic tuberculosis are considered to be non-specific reactions. In childhood the most prevalent form is phlyctenulosis. At least 80 per cent of all cases of this disease have a tuberculous basis although experimentally it is possible to excite an allergic phlyctenular reaction by sensitizing an animal to a specific chemical such as peptone or casein or to a specific organism such as the tubercle bacillus or the staphylococcus. In practice no evidence was found to show that children were sensitive to common non-microbial allergens and the difficulties in assessing sensitization to organisms other than the tubercle bacillus are considerable. A consistently great incidence of positive tuberculin reactions is found in affected children. Clinical evidence of tuberculous disease in children with phlyctenulosis is exceptional and phlyctenular ophthalmia is an uncommon manifestation in the course of tuberculosis in children. Nevertheless Sorsby emphasizes that there is considerable evidence to show that tuberculosis is implicated in the aetiology, for example in the family history and the after-history. At White Oak Hospital, London, 28 per cent of patients gave a positive family history and 5.3 per cent of children treated between 1921 and 1931 showed notifiable tuberculous disease by 1936. Summing up, Sorsby is of the opinion that phlyctenular ophthalmia is the local expression of a tuberculous infection. Chronic cyclitis and iritis are considered to have a tuberculous causal factor in many cases although there is not any conclusive proof of this relation. Ureaparotitis and sarcoidosis similarly cannot be referred indisputably to a tuberculous aetiology.

Vernal conjunctivitis

Effect of ariboflavinosis.—Castellanos describes in some detail the physical signs, aetiology and treatment of the condition now known as vernal conjunctivitis. There is considerable diversity of opinion concerning its causation and he quotes Kreibich and Dimmer who considered it to be caused by solar rays and to be comparable to other dermatoses of similar origin. By some it is held to be attributable to hay fever, anaphylaxis and other conditions. The author's own view is that a condition of ariboflavinosis is the most probable cause, this being due either to the more rapid destruction of the vitamins by the ultra-violet rays of sunlight or to the demand for a greater quantity of riboflavine during hot weather. Vernal conjunctivitis is a chronic disease often of many years' duration and affects chiefly young males during childhood and adolescence. During the winter months little disturbance is noted. In support of this opinion Castellanos gives the results of treating over 100 cases with riboflavine, 92 per cent of which showed immediate improvement. Sydenstricker's observations on the ocular manifestations are quoted; in a large proportion of cases these consisted of photophobia, burning and itching of the eyes, ocular fatigue, difficulty in far vision and amblyopia in semi-darkness. It is known that amblyopia and cataract can be produced in rats by a diet deficient in riboflavine. Thiamine, nicotinic acid and riboflavine are essential factors in the intermediate metabolism of carbohydrates and when any of the three is lacking a complex disturbance in carbohydrate metabolism results. The deficiency of riboflavine interferes with the mechanism of oxidation in the tissues; the changes in the eyes are believed to be the result of local cellular anoxaemia. The treatment is local and symptomatic, and general. In symptomatic treatment the author administers locally a few drops of a solution of 0.05 of tetracaine hydrochloride and 10 drops of epinephrine (adrenaline) hydrochloride (1 in 1,000) in 5 cubic centimetres of distilled water. The general treatment consists in the giving of 1-3 tablets of riboflavine (1 milligram each, containing 400 Sherman units) during the hot season and the recommendation to drink large quantities of milk because it is rich in riboflavine; many of the cases so treated showed improvement in all the ocular symptoms and Castellanos therefore considers that ariboflavinosis may be the cause of the condition.

Swimming-bath conjunctivitis

Clinical picture.—Derrick reports on 3 cases of inclusion conjunctivitis, the infection in all was apparently picked up at the same time when the 3 boys concerned were bathing in a swimming-pool. Outbreaks attributed to infection in swimming-baths have been described in Great Britain and in the United States of America also. The condition is caused by a filter-passing virus and the incubation period is variously given as from a few days to a few weeks. The onset is slow and one eye only is affected at the onset, the second eye being involved in from 2 to 3 weeks' time. There is a mild hyperaemia, slight swelling of the lids, painless swelling of the pre-auricular gland, photophobia and irritation. The bulbar conjunctiva remains relatively unchanged whereas the tarsal portion becomes roughened, and between the seventh and the tenth days shows the presence of follicles in closely packed formation. The inflammatory reaction dies down in 3 or 4 weeks but the mucous membrane remains thickened and hyperaemic for about 2 months. Four to 6 months later the appearance resembles folliculosis; eventually the follicles themselves disappear slowly. In the cases described by Derrick the bulbar conjunctiva was severely affected and a febrile reaction was noted in the early stage of the malady. A characteristic feature of this form of conjunctivitis is the presence of inclusion bodies in the epithelial cells. The water of the swimming-baths concerned in Derrick's cases was adequately chlorinated. Inclusion blennorrhoea can spread from patient to patient and a newly born infant may be infected from the genital canal of the mother, the epithelium of whose cervical canal has been shown to contain inclusion bodies in such instances. Similar bodies have been demonstrated in the urethral epithelium of males suffering from urethritis, these evidently contracted from an infected female during intercourse. If such

a male subject should urinate into a swimming-bath, Derrick points out, the act might lead to the contraction of an inclusion conjunctivitis by bathers.

Castellanos, L. (1944) *Arch. Ophthalm., N.Y.*, **31**, 214.

Derrick, E. H. (1943) *Med. J. Aust.*, **2**, 334.

Sorsby, A. (1944) *Practitioner*, **152**, 79.

CONSTIPATION

See also B.E.M.P., Vol. III, p. 376; Interim Supplement, No. 10*; and Cumulative Supplement, Key No. 257.

Treatment

Drugs and their limitations

Value of water, cooked vegetables and salt.—Primary constipation is independent of disease but Ditmore mentions the necessity of eliminating anal irritations which cause spasm of the sphincter. Spasm which outlasts its original cause may lead to a demand for dilatation of the muscle. The presence of pain, blood, pus or perceptible mucus indicates disease. When there is not any disease, the first necessity in treatment is water, which acts as a liquefacient, a provider of bulk and a flushing agent. Adjustment to individual requirements is necessary but a quart of water taken before breakfast over a period of from half an hour to one hour causes neither distension nor indigestion. Residue-producing vegetables constitute the second requirement. Cooked vegetables eaten twice daily are essential, and salads, tomatoes, potatoes and vegetable soups must not be substituted for cooked fibrous and leafy vegetables. The third desideratum is the freer intake of salt which, although contra-indicated in certain diseases, may offer to normal individuals benefits additional to the relief of constipation. Ditmore condemns laxatives and states that bulk-producing products, which are sometimes irritating, soon lose effect. Mineral oil by injection is insanitary and deleterious but tablespoon doses by the mouth receive faint praise as a fourth step. Mineral oil should be taken before each meal if the daily evacuation has not occurred but should never be taken at bedtime. Frequent evacuations and leakage accompany overdosage. Prolonged constipation dulls reflex response to a loaded rectum and an attempt at defaecation should follow soon after water has been taken. With the re-establishment of habit, the urge to defaecate returns. The steps recommended abolish the need of laxatives.

Ditmore, D. C. (1943) *Amer. J. digest. Dis.*, **10**, 356.

CONVULSIONS IN INFANCY AND CHILDHOOD

See also B.E.M.P., Vol. III, p. 406; and Cumulative Supplement, Key No. 259.

Treatment

Treatment of underlying causes

Effect of subdural haematoma.—Subdural haematoma in infancy is a common condition during the first two years of life, and Ingraham and Matson have encountered 98 cases in 65 months. Injury is probably always a factor in the aetiology of the lesion but if the injury is trivial it may escape notice. In the authors' cases history of injury was obtainable in 52 cases only, including 28 babies who had experienced severe trauma at birth. Fracture was detected 11 times radiographically. Falls on the head rather than glancing blows disarrange the cranial contents and rupture veins which enter the longitudinal sinus; the common occurrence of bilateral lesions suggests such a general shift of intracranial contents. Moulding during labour has a similar effect. The influence of a bleeding diathesis from deficiency of vitamins C and K is indeterminate. Phenomena suggestive of subdural haematoma are pyrexia, convulsions, vomiting, infection, hyperirritability, stupor, anaemia, scurvy and subnormal temperature. Investigation may reveal hyperactive reflexes, bulging fontanelles, cephalic enlargement, abnormal fundi and paralysis. Subdural puncture alone enables certain diagnosis to be made. In this series puncture yielded sanguineous fluid in 88 cases and clear fluid, highly albuminous, in 10. The differential diagnosis of hydrocephalus and subdural haematoma is highly important. Most cases of haematoma occur during the first 6 months of life. The authors estimate that 34 infants were seen within a week of symptoms, 21 within a month and 27 within 6 months. Delay in seeking advice in 5 cases exceeded 6 months; the outlook was correspondingly graver. Clots, with a membranous sac—which were seen in 62 cases—may cover the entire brain with the exclusion of the occipital pole. The rapid expansion of the infantile brain necessitates the removal of the constricting membranous sac—evacuation of its contents is insufficient. Gradual decompression is essential and begins with the diagnostic puncture. The needle is introduced vertically, through a novocain (procaine hydrochloride) wheal, in the frontal suture and at first, bilaterally. If a bilateral haematoma is detected subsequent tapplings are performed daily for about a fortnight on alternate sides, some 15 cubic centimetres of fluid being withdrawn on each occasion. Next, through incisions in the temporal muscles burr holes are made in order to complete drainage and to determine the existence of membranes. If their presence is established they are removed a week later by craniotomy. Nine of the 88 patients died in hospital. Of 57 patients whose later history is known 13 are mentally retarded or deficient but 44 are normal children.

Ingraham, F. D., and Matson, D. D. (1944) *J. Pediat.*, **24**, 1.

CORNEA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 424; and Cumulative Supplement, Key No. 260.

Injuries*Foreign bodies*

Treatment with silver nitrate.—Gillette recommends the local application of silver nitrate as an aid to the removal of foreign bodies from the cornea. The method is applicable to all foreign particles but the author is chiefly concerned with the foreign bodies encountered in industry. These usually have an iron content and quickly produce a rust stain the removal of which from the tissues of the eye often results in considerable damage. Moreover the foreign bodies are usually hot and cause a burn when they strike the cornea. Gillette applies a 1–3 per cent solution of silver nitrate to the foreign body and the surrounding epithelium; the solution is applied by means of a small thread of cotton spun on the sharpened end of a round wooden toothpick. The reaction is a faint, grey swelling of the superficial epithelium which elevates the foreign body slightly above the level of the surrounding epithelium. The injured eye is first anaesthetized with a drop of 0.5 per cent solution of tetracaine hydrochloride (amethocaine hydrochloride) at one-minute intervals. The slit lamp is used to locate any minute particles which cannot be satisfactorily seen with the loupe. The conjunctival sac is irrigated with a mild solution of mercuric oxycyanide and fluorescein is instilled if necessary. The silver nitrate solution is then applied and the author employs the sharpened end of a round toothpick, which has been sterilized, for the purpose of removing the foreign body, burn and stain. When the stain does not readily come away the point of a cystotome is used. This is preferable to other instruments. The silver nitrate procedure is not employed when Bowman's membrane is injured. White's tar paste (coal tar, zinc oxide and soft paraffin) or sulphathiazole ointment is instilled immediately after removal of the foreign body. Ulcers are cleaned with tincture of metaphen and filled with sulphathiazole powder; sulphathiazole ointment is subsequently prescribed.

Ulcers*Treatment of ulcers*

Experiments in lesions set up by different organisms.—Robson experimentally produced lesions of the cornea in animals by the use of several varieties of organisms and he tested the effects of different forms of therapy. In local therapy, if one eye is left untreated it serves as a control. A 30 per cent solution of sodium sulphacetamide (albicid soluble) was found effective in *Bacillus pyocyaneus* infections. Numerous strains of the pneumococcus failed to produce ulceration after injection and resulted only in infiltrates; type XIX however gave rise to ulceration, iritis and hypopyon and frequently to septicaemia. The best results in pneumococcal infections were obtained with penicillin applied locally every hour, although striking results were also seen with sodium sulphacetamide. Sodium sulphapyridine appeared to be of some value but the solution is alkaline, and alkaline solutions in general have an irritative action on the conjunctiva and also interfere with the natural lysozyme of the tears which produces its maximum antibacterial effect at the same reaction as that of the body. Local applications of penicillin were very effective in lesions secondary to injections of coagulase positive strains of staphylococci; sodium sulphacetamide was also very valuable but somewhat less so than was penicillin. Strangely enough, sulphathiazole, applied either as a powder or in solution, was without effect. Certain strains of haemolytic streptococci produced ulcers, and again penicillin proved its value in treatment whereas sulphonamides were ineffective. Throughout these experiments the importance of early treatment was emphasized and upheld, since if it was given within a very short time of the inoculation the lesion could usually be prevented. Proflavine was found to be of comparatively little value in pneumococcal, staphylococcal and streptococcal lesions. Experiments have been started on tuberculous corneal ulcerations but are as yet incomplete.

Hypopyon

Treatment by albucid and proflavine.—Trevor-Roper describes the results of treatment of hypopyon ulcers with albucid and proflavine. Albucid is an effective bactericide when it is introduced into the conjunctival sac and penetrates the corneal tissues well. The 12 cases treated with albucid had 30 per cent drops instilled hourly by day and 10 per cent ointment applied 4-hourly by night for 4 days; 10 per cent ointment was used thrice daily thereafter. In 4 cases the glass shell container was employed so as to keep the albucid solution in contact with the eye for a longer time, but the pain induced rendered its use impossible. The hypopyon cleared up in 6 cases within an average period of 5.3 days, Saemisch's section was required in 3, and in the remaining 3 hypopyon was still present when the patients were transferred to a base hospital within respectively 3, 21 and 42 days. Since the results were not considered to be encouraging, the author in another series of 12 cases adopted treatment with irrigations of proflavine. He used an 0.1 per cent solution in saline, 2-hourly by day and 4-hourly by night. The hypopyon cleared up in an average of 2 days, but 3 cases required a Saemisch's section. In these latter the age was over 60 years; of the 3 Saemisch's section cases of the albucid series, 2 were octogenarians and both lost the eye. Three cases of hypopyon iritis responded satisfactorily to the proflavine regimen. One case of hypopyon ulcer was treated with oral sulphapyridine but evisceration was necessary after 16 days. For all patients atropine, heat, diathermy, covering and rest were used in addition to the specific drug mentioned.

Leucoma

Treatment by corneal transplantation.—In a paper read before the Chicago Ophthalmological Society Perritt summarizes his experiences of corneal transplantation. At first he used an apron conjunctival flap but this was discarded for various reasons. The recipient cornea is bevelled approximately at an angle of 25° but the corneal implant is not bevelled because if this is done curling of the endothelium results with gradual formation of scar tissue at the line of junction. The Castroviejo trephine is employed. A special type of corneal suture has been devised. The material used for the implant has been obtained from still-born infants, from children dying within a few days of delivery or from adult eyes freshly enucleated on account of injury or disease. The results have been equal whatever the source of the graft provided that the corneal epithelium and endothelium were normal. The eye can be kept in a special refrigerator for a period up to 48 hours; it is examined with a slit lamp just before being used. Glaucoma contra-indicates the operation. When partial staphyloma or ectatic leucoma is present the prognosis is very unfavourable. The fate of the transplant is influenced chiefly by the character of the leucoma, the prognosis being better if corneal elements remain. Favourable situations are those in which disease is limited to the cornea, in which the corneal leucoma is not very dense and is surrounded by clear areas and in which the tension is normal. Unfavourable situations are those in which a dense leucoma extends over almost the entire cornea, in which aphakia is present, in which tension is increased or in which corneal cloudiness with pannus formation has developed. In such cases preliminary operations must be performed to prepare the ground for keratoplasty. Corneal transplantation is sometimes done in a blind eye for cosmetic effect alone. Of 11 patients operated on 6 regained useful vision.

Symptomatic affections**Interstitial keratitis**

Treatment with vitamins E and B complex.—Stone describes the treatment of 10 patients with advanced interstitial keratitis with vitamin E (wheat-germ oil) and vitamin B complex, administered at first in the form of a mixture consisting of 1 part oil to 3 parts vitamin B complex, in doses of from 8 to 12 cubic centimetres daily. The vitamin B complex was added on account of its synergistic action with vitamin E. Later, on the introduction of wheat-germ oil concentrates, 50-milligram mixed tocopherol capsules (Lilly) or (Winthrop) were given instead, 1 capsule once or twice daily, usually with 1 or 2 capsules of vitamin B complex. The resistance of interstitial keratitis to antisyphilitic treatment suggested the presence of other causal factors besides the spirochaetal invasion, and the beneficial effect of vitamin E on the rate of absorption, observed in the case of other tissue exudates, prompted its use in the treatment of interstitial keratitis. All the patients had severe limitation of vision in one or in both eyes, with photophobia, vascular congestion and superficial and deep corneal opacities, and had received ample antisyphilitic therapy of various kinds without benefit to the eye condition. In cases of long standing the administration of vitamin B over a period of from 12 to 18 months produced gradual and continuous clearing of the cornea with return to normal vision. In one case of short duration, absorption of corneal exudates was complete after 4 weeks of treatment by vitamin therapy. Vitamin E also helped to relieve photophobia and to reduce excessive corneal vascularization and circumcorneal congestion. Riboflavine alone or in combination with vitamin E was primarily effective in relieving photophobia and in reducing the extent of circumcorneal infection and capillary proliferation, but had apparently no effect on the rate of absorption of corneal opacities and scars.

Corneal vascularization

Association with riboflavine deficiency.—The deficient absorption of riboflavine (vitamin B₂) is a suggested cause of corneal vascularization. Since vascularization connotes the formation of new channels, Vail and Ascher contend that the term is here a misnomer. Newly formed capillaries were found only in cases of antecedent corneal disease. The authors' observations were concentrated on the limbal vascular meshwork pervading the conjunctivo-scleral wedge the apex of which lies at the termination of Bowman's membrane, the base abutting on the episcleral tissue and on the superficial part of the sclera. Normally each limbal loop possesses an afferent and an efferent limb. In congestion, many afferent and very few efferent vessels were visible in each quadrant of the limbal circle. These efferent vessels are not new formations. They are already existing channels of the meshwork enlarged and engorged by their function of returning the blood from one entire limbal quadrant to the larger conjunctival veins. The blood flow in them is from above downwards and from below upwards to the horizontal meridian. It is proposed to designate the channels concentric collaterals. Evidence was against a correlation between the presence of concentric collaterals and vitamin deficiency. From a nutrition clinic 85 patients with known or suspected deficiency of riboflavine, nicotinic acid or thiamin were referred for ophthalmic examination. Only one-eighth of the 85 displayed concentric collaterals as against one-third of 69 unselected patients examined in an eye clinic. In both groups many more females were affected than were males and more ill-fed persons than well-fed; age was without influence. These facts acquit vitamin deficiency of responsibility for causing concentric collaterals.

Gillette, D. F. (1944) *Arch. Ophthalm., N.Y.*, **31**, 129.

Perritt, R. A. (1943) *Arch. Ophthalm., N.Y.*, **30**, 14.

Robson, J. M. (1944) *Brit. J. Ophthalm.*, **28**, 15.

- Stone, S. (1943) *Arch. Ophthalm., N.Y.*, **30**, 467.
 Trevor-Roper, P. D. (1944) *Brit. J. Ophthalm.*, **28**, 181.
 Vail, D., and Ascher, K. W. (1943) *Amer. J. Ophthalm.*, **28**, 1025.

DEAFNESS

See also B.E.M.P., Vol. III, p. 555; and Cumulative Supplement, Key No. 284.

Anatomy of the ear

Function of parts of the ear

The cochlea and electrical responses.—The auditory significance of the electrical response from the cochlea is analysed by Kellaway, who takes as his starting-point the phenomenon observed by Wever and Bray. These observers placed electrodes connected with a loud speaker on the auditory nerve of a cat. Words spoken into the cat's ear were reproduced with such fidelity that the speaker was identifiable by his voice. This phenomenon prevails in other mammals, is correlated with the evolutionary level of the sense organ and therefore diminishes in birds and reptiles. It was attributed by these observers to action currents in the auditory nerve. Others suspected its divisibility into a cochlear portion and a portion inherent in the auditory nerve, and among other evidence adduced the following proofs. (1) Action potentials of the auditory nerve disappear immediately at death but cochlear potentials survive death for some minutes. (2) Action potentials reproduce frequencies in excess of 1,000 cycles per second inaccurately whereas cochlear potentials faithfully reproduce tones throughout the audible register. (3) Narcotics and deep anaesthesia suppress action potentials whereas cochlear potentials are suppressed only by destruction of the blood supply or the basilar membrane. The origin of the cochlear portion was next traced to the organ of Corti, by the use of albino cats as subjects. In them there is not an organ of Corti and similarly the audio-electric response to sound stimuli is absent. Evidence further confines the origin of cochlear potentials to the hair cells. Clinically their degeneration, without other abnormality, has been demonstrated in boiler-maker's deafness; experimentally, such degeneration in the waltzing guinea-pig inhibits cochlear response. It is suggested that the mechanical vibrations of sound stimulus which impinge on the tympanum are converted by piezo-electric influence, acting through the hair cells, into electrical energy. The cochlear response is an index of the peripheral processes involved in hearing, but interpretation of it is limited by an understanding of central processes which is at present insufficient.

Types of deafness

Resulting from explosions

There are according to Suggit three clinical types of deafness produced by gunfire and explosives. (1) Middle ear deafness; (2) a gradual high tone loss due to prolonged damage of the cochlea; (3) an abrupt high tone loss due to blast concussion. In (1) there is usually rupture of the eardrum with bleeding. This is probably caused by blast, which produces a wave of increased pressure followed by a suction wave. Loss of hearing is that of middle ear type with a negative Rinne. Recovery in Suggit's case was almost complete in 56 days, except for the 8,000–13,000 frequency zone. Most patients recover completely unless the cochlea is also injured; then the high tone loss is permanent. In (2) after prolonged exposure to gunfire there is cochlear deafness, with a gradually falling curve from lower to high tones in the audiogram. Typical of these cases of 'occupational deafness' is a dip in the audiogram at 4,000 cycles. Unless the patient is removed from trauma, the high tone hearing loss may be permanent. (3) In Suggit's series of 69 cases, 26 were of concussion deafness with abrupt high tone losses. This may be produced by a single explosion such as the muzzle blast of a high-powered rifle. The audiogram is quite different from that of the two previous types. A sudden sharp drop in the audiogram occurs between 1,000 and 2,000 cycles or between 2,000 and 4,000 cycles. In severe injuries the drop is closer to the lower frequencies and in lesser injuries is more towards the higher frequencies. Tinnitus is frequent and labyrinthine irritation may be present in one or two cases. In the gradual type of high tone deafness there is degeneration of the organ of Corti. Effective plugging of the external auditory meatus affords some little protection, but the wearing of antiblast helmets containing telephones would afford better protection for gun crews in the Navy.

Diagnosis

Nerve deafness

Association with retinitis pigmentosa.—Sirls and Slaughter have examined the hearing of 12 persons suffering from retinitis pigmentosa, a condition known to be frequently associated with deafness. Cases presenting evidence of any local disease which might cause deafness were excluded. Of the 12 patients 6 were deaf, as was shown by audiograms, and in all these 6 the deafness was of the nerve type. Only 4 of them had noticed any impairment of hearing, a fact which confirms the authors' suspicion that the incidence of deafness in retinitis pigmentosa is higher than has generally been supposed. No relation could be demonstrated between the onset or the severity of the visual and the auditory symptoms. Since the retina and the inner ear are both developed from the neuro-ectoderm of the primitive brain, it may be supposed that a common germ-plasm defect accounts for the changes in the eye and ear found in retinitis pigmentosa.

Mass irrigation tests.—Vastine has studied the correlation between hearing and vestibular function in deaf adolescents. Audiometric and vestibular tests were carried out on 408 ears of 208 pupils at the Pennsylvania School for the Deaf. The ages of the subjects ranged from 14 to 19 years. For vestibular examination the Bárány caloric or mass irrigation test was used, and the time from the beginning of the douching with water at 68° F. to the onset of nystagmus was noted. Only ears with intact drums were tested. The reaction was classified as 'normal' when nystagmus was produced within 55 seconds, as 'moderately hypo-active' when the time was from 55 seconds to 2 minutes and as 'markedly hypo-active' when the reaction time was longer than 2 minutes. If no nystagmus occurred after 4 minutes' douching the labyrinth was considered 'inactive'. The results showed that complete loss of vestibular function is comparatively rare in deaf young people. Function was subnormal in 57 per cent but absence of function was noted in only 19 per cent. In general, decrease of vestibular activity was found to run parallel with decrease of acoustic activity. The 24 per cent of ears yielding normal vestibular reactions showed a median threshold for each auditory frequency at a lower intensity level than that shown by ears with hypo-active vestibular function; more than half of these ears reacted to the first 5 auditory frequencies. An exception was noted in 2 pupils with bilateral vestibular inactivity, in each of whom one ear failed to respond to any frequency whereas the other reacted to all frequencies except 8,192 cycles. In both pupils the deafness was caused by meningitis, which is thus shown to be capable of selective destruction of the static labyrinth.

Otosclerosis

Fluorine as a cause.—The theory that fluorine deficiency may be a primary cause of deafness associated with otosclerosis and fibrosis is postulated by Lewy. It has long been known that pathological changes in the teeth may occur from the habitual drinking of water containing two parts or more of fluorine per million; on the other hand, when fluorine is present in the drinking-water in less than toxic concentration, the incidence of dental caries in a community is greatly lowered. These observations led the author to test audiometrically the hearing of schoolchildren in 68 counties of Illinois. Among a total of 132,572 children examined, 5,406 or 4.7 per cent showed defective hearing. In the counties in which the drinking-water does not contain any fluorine 109,869 children were examined; the number with defective hearing was 5,406 or 4.9 per cent. In 4 counties, in which the drinking-water contains fluorine in the proportion of 1.4 parts or less per million, 20,488 children were examined and 574 (2.8 per cent) showed defective hearing. It is believed that fluorine acts upon the metabolism of bone, possibly through the medium of the parathyroid glands. A suggestion has been made that the influence of fluorine upon the incidence of dental caries and otosclerosis should be tested by adding non-toxic amounts (say 0.8 part per million) of fluorine to the public water supply of a community whose water is at present fluorine-free. It would be necessary for the experiment to be continued for a period of 10 or 12 years.

Treatment

Hearing aids

Essentials in design.—Grossman discusses the acoustic properties of the external meatus and middle ear with reference to the fitting of hearing aids. He has observed that the present design of the earpiece causes serious loss in the upper frequencies, a matter of particular importance in perceptive deafness. Experiments with 3 ear moulds were carried out in a normal person. The first mould was of the type ordinarily used, with a sound-conveying canal measuring 3 millimetres in diameter; the second had a canal diameter of 1.5 millimetres; the third had a diameter of 5 millimetres. It was found that when subjected to identical tests the results yielded by the three moulds were quite different, much the closest approximation to the natural sound of the voice being obtained with mould (3), that is the mould interfering least with the normal dimensions of the aural canal. The form of the resonance curve depends not only on the density of the medium through which sound passes, but also upon the length and cross-sectional area of the external canal and the impedance of the drum. For perceptive deafness the mould should be as large and straight as possible, and it is advantageous to introduce an acoustic high-pass filter, in the form of a short tube with a side branch orifice, between the receiver and the mould. For middle ear deafness the mould should have a long tip and the diameter of the sound-conveying canal should be not less than 3 millimetres.

Grossman, F. M. (1943) *Arch. Otolaryng., Chicago*, **38**, 101.

Kellaway, P. (1944) *Arch. Otolaryng., Chicago*, **39**, 203.

Lewy, A. (1944) *Arch. Otolaryng., Chicago*, **39**, 152.

Sirles, W. A., and Slaughter, H. (1943) *Amer. J. Ophthalm.*, **28**, 961.

Suggit, S. (1943) *J. Laryng.*, **58**, 313.

Vastine, Mary F. (1944) *Arch. Otolaryng., Chicago*, **39**, 164.

DEATH, SUDDEN AND UNEXPECTED

See also B.E.M.P., Vol. III, p. 565.

Other causes of sudden death

Diffuse fatty degeneration of the liver

Graham calls attention to a little-known form of sudden death. It is one which occurs in young adults, in whom at necropsy the only significant pathological lesion is a large diffusely

fatty liver. Almost invariably there is a history of chronic alcoholism. He emphasizes, however, the fact that the history and chemical analysis show that the patients usually had not taken alcohol near the time of death. In typical cases death results with extreme speed and with little or no warning. He reports 11 cases all occurring within one year. In 5 of them the sole pathological lesion at necropsy was a diffusely fatty liver. In 6 other similar cases some additional lesion, which could be regarded as a cause or main contributory cause of death, was found at necropsy. Graham does not claim to give any adequate explanation of the mechanism of death, but suggests that a vitamin deficiency with or without hypoglycaemia might be responsible. Neither does he imply that all persons with such a liver condition die suddenly or unexpectedly. Of the 11 entirely unexplained deaths, none occurred between late June and late September. This rules out heat stroke. The economic and social status of the patients were above the average. Of the 5 patients with fatty liver as the sole lesion at necropsy, 3 had attacks of unconsciousness before death. One had vague symptoms of weakness and anorexia for a few months before death. In 3 cases death occurred within half an hour from the time of collapse. In the fourth, death occurred during sleep and in the fifth there was a period of coma lasting from 2 to 3 hours. In 3 of the cases there were not any normal liver cells found on microscopic examination. Each liver cell was variably distended with a fat globule. In some the globules were so large as to compress the nuclei into a crescent shape. In the other 2 cases the picture was only slightly less well defined. The most striking clinical feature was the lack of specific clinical signs or symptoms. Although in 4 patients a coronary death was simulated, the most careful search showed no heart lesion. Of the 6 cases which at necropsy showed some other lesion in addition to the enlarged fatty liver, 4 had a terminal aspiration pneumonia. In 2 there was an early haemorrhagic pancreatitis. In 5 of the 6 there was a history of alcoholism, but only one was intoxicated at the time of death.

Graham, R. L. (1944) *Johns Hopk. Hosp. Bull.*, 74, 16.

DENGUE

See also B.E.M.P., Vol. III, p. 587.

Clinical picture

Circulatory system

Effect of virus factor.—Hyman records observations made on dengue occurring among members of the United States Navy and marine combat units in the South Pacific. Dengue occurs mainly in the Tropics and is a virus disease transmitted by the *Aedes aegypti* mosquito. The signs and symptoms in several ways resemble those of epidemic influenza, and include headache, a rash, leucopenia and bradycardia. In the epidemic in the above-named area there were many serious cases which were clinically different from those previously recorded. The leucopenia was variable and it was noted that in some cases in which there was a slow return to a normal leucocyte count there was also considerable weakness and physical depression. The subsequent asthenia often persisted for some weeks. The slow pulse rate appeared to be due to simple sinus bradycardia. The electrocardiograms taken of the patients were not abnormal in any age group although there were some disturbances of conduction and of rhythm. Radiological examination of the heart did not show any consistent abnormalities. The blood pressures of the patients were generally low, especially when asthenia was pronounced. The hearts showed significant changes. The sounds were of poor quality and a few inconstant murmurs were heard. Over the radial artery the pulse appeared to be dicrotic with a considerable spread of the two waves. It was modified both by exertion and by administration of belladonna. It is suggested that the virus factor of dengue chiefly affects the autonomic nervous system and causes an extreme vagotonic reaction which would account for the associated bradycardia hypotension and general neuromuscular depression. The cardiac syndrome resembles that seen in post-influenzal cardiac disturbances; the use of belladonna or atropine may be of value to counteract the vagotonic symptoms in both diseases. In the author's cases the depression seemed to be relieved by the administration of belladonna and vitamins. At present there is not any specific treatment for dengue fever.

Dengue of South Pacific area

Characteristics of the disease.—Cavanagh describes the features of dengue as encountered in the South Pacific area. Dengue varies in its characteristics in different parts of the world. In the South Pacific area it is a self-limited disease, has an acute onset, and lasts from 6 to 11 days. After 2 or 3 days the initial temperature subsides and a morbilliform eruption usually develops; within 24 hours the temperature rises again and drops by crisis after from 2 to 3 days. The severity of the disease in Cavanagh's cases varied. Backache, prostration, pain behind the eye-balls, frontal headache and anorexia were the commonest symptoms. A bad taste in the mouth which Cavanagh designates the 'dengue taste' was characteristic. Joint pains occurred in 70 per cent of cases but were unassociated with articular swelling. Nausea, chills, sore throat and pruritus in the period of desquamation were also features. Physical examination revealed little except lymphadenopathy and rash; bradycardia was common. The posterior cervical, anterior cervical, epitrochlear, axillary and inguinal glands were affected in that order. In only 2 cases did the glands suppurate. A rash was seen in about half the number of cases and was morbilliform in character. The trunk was most frequently involved but in the more severe cases the extremities were also; the rash was often haemor-

rhagic in the legs. The 'double hump curve' was seen in 51 per cent of cases, but temperature patterns resembling those of malaria were also found. Meningismus was not unusual in severely ill patients. A lowered leucocyte count was the most characteristic laboratory finding; the differential count was in no way characteristic, but the reduction was in almost all cases at the expense of the granular cells. The disease was transmitted by the *Aedes aegypti* mosquito. The author's observations agreed with the recognized incubation period of from 7 to 10 days. Complications were unusual and varied. Diagnosis is easy during an epidemic; measles and malaria are the conditions most likely to be confused with dengue. Prophylactic measures included the use of mosquito netting and the spraying of living quarters and fox holes; the men were required to be fully clad at all times and to report immediately to the officer of the day if they did not feel well. Treatment is symptomatic.

Occurrence in U.S. Army.

Kisner and Lisansky analyse 318 cases of dengue fever which occurred among non-immune men in the United States Army who had newly arrived on a South Pacific island. This fever is an acute infectious disease caused by a specific filter-passing virus which is transmitted by the bite of female mosquitoes, mainly of the *Aedes aegypti* and *Aedes albopictus* species. In this instance the *Aedes aegypti* was the agent. After an incubation period of from 6 to 10 days, the onset of the disease was sudden in nearly all the cases, feverishness and chilliness being an early and common symptom. Ninety-nine per cent complained of aches and pains in one or more sites or generalized. A relative bradycardia was found in 97 per cent. The temperature curve in two-thirds of the cases was 'saddle-back' in character; there was a primary rise to a maximum of 104° F. for 3 or 4 days, 1-2 days' intermission or remission and then a secondary rise for 2 or 3 days before the final return to the normal. The remaining one-third showed a single elevation of temperature which lasted 5-6 days. A rash, variable in time and site of appearance but usually of a widespread, blotchy and erythematous character, developed in 37 per cent of the patients. In every case the patient had a leucopenia and a Schilling shift to the left. All the patients responded to symptomatic treatment and made complete and uncomplicated recoveries; pathological investigation *post-mortem* was therefore precluded. The authors consider that susceptibility to the infection is universal and that the immunity conferred by an attack lasts for from 5 to 10 months.

Cavanagh, J. R. (1943) *War Med.*, **4**, 549.

Hyman, A. S. (1943) *War Med.*, **4**, 497.

Kisner, P., and Lisansky, E. T. (1944) *Ann. intern. Med.*, **20**, 41.

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED-ERUPTIONS

See also B.E.M.P., Vol. III, p. 609; and Cumulative Supplement, Key No. 290.

Externally applied agencies: direct exposure

Toxic dermatitis

Associated with boots and shoes.—It has long been recognized that, owing to their sensitizing and skin-irritant properties certain compounds—such as anti-mildew preparations, dyes, glues and substitute materials—which are used in the manufacture or cleaning of footwear, sometimes cause a dermatitis of the feet. Shaw encountered 22 such cases in practice within 3 years; he suggests that the condition is not as rare as it is ordinarily supposed to be. The eruption—a scaling erythema usually accompanied by vesicles and papules—may be differentiated from fungoid infection, with which it is frequently confused, by the following salient features. (1) It appears shortly after wearing (and disappears after discarding) new or freshly dyed shoes, patch tests of material from which will give positive reactions. (2) The condition fails to yield to treatment appropriate to fungoid infection and cultures and microscopic examination fail to demonstrate such infection. (3) The itching, which may appear before the eruption, is disproportionately severe. (4) The area of skin affected is sharply outlined; it is most evident on the dorsal surface of the feet and larger toes and there is not any involvement of the interdigital spaces. (5) When boots have been worn the ankles too are generally affected. A change in the brand of footwear is usually the only treatment which is required. Symmetric lividity of the feet may possibly be confused with a dermatitis due to shoes. In the former condition however bromidrosis, hyperidrosis and well defined erythematous plaques—soggy and thickened but lacking true vesiculation—on the soles of both feet, serve to establish the diagnosis.

Dermatoses in soldiers.—Davies and Barker report on 201 cases of dermatoses in soldiers wholly or partly due to skin intolerance of contact with woollen textiles, proved by patch tests and the effect of resuming khaki clothing. Many cases were seen in soldiers with scabies who relapsed persistently or failed to respond to treatment. The patient usually complained of itching, which was often worse by day. Parts exposed to contact with khaki serge or other woollens are chiefly involved. In every case the lower extremities are attacked with increasing intensity towards the tops of the boots. In the most important group there is prurigo simulating scabies. The eruption increases towards the ankles, itching is severe by day, and acarine material is not found. Gonadal deficiency plays a part in many cases. Some milder cases responded dramatically to administration of ascorbic acid, but severe cases did not. Sensitization may occur spontaneously from friction by garments in association with sweating, but

DERMATITIS DUE TO INJURY AND POISONING—DIABETES MELLITUS 169

usually its onset is determined by another dermatosis such as scabies or arsenical dermatitis. Anti-vermin impregnation of battle-dress is often an aetiological factor. Treatment consists primarily in removal of the irritant. The patient should sleep between sheets, have a cotton shirt, and wear cotton pyjamas by day. The application of simple remedies like calamine liniment or lotion is helpful. Pyodermatic lesions should be covered with disks of elastoplast. Sweating must be avoided and sleep ensured. The impression is that lapse of time is the most important therapeutic factor. Cases of long standing with strongly positive patch tests must be regarded as incurable. Mild cases of the prurigo type recover slowly. In moderately severe cases patients do not lose their symptoms or rash completely, but if protected by cotton they may be returned to duty without necessarily becoming worse. Generally they relapse and have eventually to be invalided out of the Forces.

Feigned eruptions

Diagnosis

Main points.—Discussing factitious eruptions of the skin, Smith points out that most are self-inflicted but that in rare instances they may be inflicted by another person. The patients are usually young women who are either malingerers or psychoneurotics. The malingerer is as a rule the less easily detected. The psychoneurotics are usually either physically healthy young women who may show hysterical stigmata such as anaesthetic areas in the skin or anaesthesia of the palate, or anxious neurasthenic women craving for rest and sympathy. The lesions may be caused by a number of agents, mechanical and chemical. Their character and distribution are unlike those of any genuine disease. They are asymmetrical, appear suddenly in normal skin within easy reach of the hands, are oval, angular or linear rather than rounded in shape and show no shading off at the margins. None of the known primary lesions are found in or around them. In most cases the diagnosis is immediately obvious. The only disease which may simulate dermatitis autophytica is erysipeloid, which occurs in people handling raw meat. Successful management of the patient includes diagnosis and treatment of the mental state. Locally the best treatment is an occlusive dressing with splinting if necessary.

Davies, J. H. T., and Barker, A. N. (1944) *Brit. J. Derm.*, **56**, 33.

Shaw, C. (1944) *Arch. Derm. Syph.*, N.Y., **49**, 191.

Smith, S. W. (1943) *Practitioner*, **151**, 33.

DERMATITIS HERPETIFORMIS

See also B.E.M.P., Vol. III, p. 627.

Morbid anatomy

Eosinophilia

Comparison of eosinophils in tissue and blood.—Burkhart and Montgomery report on work done in order to find out whether or not there is any relation between eosinophilia in the tissues and eosinophilia in the blood in some of the skin diseases which cause tissue eosinophilia. In all, 9 cases of dermatitis herpetiformis and 3 cases of pemphigus vegetans from which histological sections were obtained were studied, also 76 cases of localized neurodermatitis and 61 of disseminated neurodermatitis. Special attention was given to the number of lobes in the eosinophil nucleus. The authors state that eosinophils are formed in the bone marrow and enter the circulation as mature cells; but there is also good evidence that eosinophils are formed in the tissues. Eosinophils have positive chemotaxis and are phagocytic. Patients with a high percentage of eosinophils in the blood are more likely to have a local tissue eosinophilia after the injection of a foreign protein than are those with a normal percentage. In localized neurodermatitis it is unusual to find a high blood eosinophilia or to find eosinophils in the affected skin tissue. Disseminated neurodermatitis and to a lesser extent exudative neurodermatitis tend to produce an increase in blood eosinophils as well as numerous eosinophils in the affected skin. Eosinophils occur in the cutis in dermatitis herpetiformis and pemphigus vegetans as well as in the bullae and abscesses in the epidermis. No differential blood count could be made in some cases in these groups. Eosinophils with bilobed nuclei usually predominate over those with nuclei with one lobe in the tissue infiltrate in cases of localized neurodermatitis, disseminated neurodermatitis or dermatitis herpetiformis and in all cases of exudative neurodermatitis.

Burkhart, R. J., and Montgomery, H. (1944) *Arch. Derm. Syph.*, N.Y., **49**, 19.

DIABETES MELLITUS

See also B.E.M.P., Vol. III, p. 644; and Cumulative Supplement, Key No. 296.

Diabetes mellitus

Aetiology

Is alloxan a cause?—In a study of the diabetogenic action of alloxan, Hughes, Ware and Young were able to confirm the work of other observers that a single injection of alloxan (a simple condensation product of urea and mesoxalic acid) may cause necrosis of the islet cells in the pancreas of the rat and of the rabbit. In the case of the latter they also confirmed that persistent glycosuria was a later development after the injection and that a condition similar

to that of diabetes mellitus also followed. In one rabbit killed after being diabetic for 3 months the authors did not find any islet tissue at all. When 10 units of protamine zinc insulin was administered to fasting rabbits, there was a fall of blood sugar level which finally resembled that which resulted from intravenous injection of 200 milligrams of alloxan per kilogram of body weight, and finally the animal became convulsed. When the rabbit was not fasting and was allowed to eat throughout the experiments, the hypoglycaemic effect of administration of 10 units of protamine zinc insulin was lessened by about the same amount as was that of alloxan. The results suggest that the hypoglycaemic action of alloxan may be due to the slow release of pre-formed insulin from dying islet cells. This theory presupposes that there has not been any extensive liver damage such as would produce hypoglycaemia of hepatic origin. If it is true that alloxan can be present in human urine under pathological conditions, diabetes mellitus might arise from a metabolic disorder which induced the production of free alloxan in the body.

Morbid anatomy

Amyloidosis.—In a recent investigation Ahronheim shows that the term, hyaline fibrosis, used in reference to the islands of Langerhans in the pancreas is inaccurate, as the 'hyaline' substance often found in the pancreatic islands is now believed to be amyloid. Other organs may not contain amyloid even when it is found in the islands yet in generalized amyloidosis the pancreas may not be involved at all. In diabetic and non-diabetic patients who are amyloid positive a condition of hypertension is common. The pathological condition of highly vascular islands may interfere with the circulation and may thus cause a hypertension similar to the renal hypertension which is caused by diseased renal glomeruli. The author suggests that changes in diabetes mellitus and in pre-diabetic states may render the islands susceptible to amyloid deposition. He does not consider that amyloidosis is diagnostic of diabetes mellitus or that it causes diabetes. That individuals of middle age who suffer from glycosuria are liable to amyloidosis of the islands of Langerhans; the condition is seen less often in the older, thin diabetic individuals. The author makes an interesting observation about juvenile diabetes: it is, he states, a disease distinct from diabetes of the adult. Amyloid insular degeneration is rarely seen in juvenile diabetics and in some quoted instances in which it had been found the patients had died from advanced pulmonary tuberculosis which might have also caused the amyloidosis.

Clinical picture

Associated with Addison's disease.—Nix, who reports the association of diabetes mellitus with Addison's disease in a man aged 39 years, points out the rarity of the association and the interest that was attached to the influence of adrenal metabolism 30 years ago by Britton and Silvette. Nix was able to collect only 8 unequivocal recorded cases and this additional example appears to be the first to be published in Canada. The symptoms antedated death by 6 or 8 weeks and were those of acute adrenal cortical insufficiency, severe asthenia, hypotension, mild pigmentation, anorexia, nausea and small heart. Pigmentation in Addison's disease is stated to be often at first yellow as in this case but the presence of the disease was not thought of until necropsy revealed it. The onset of weakness and fatigue dated back to 2 months before death and after a loss of weight of 20 pounds. The necropsy showed absence of one adrenal gland and true fibroid atrophy of the other.

Diagnosis

Phloridzin tests.—Korenberg points out that if the renal threshold for sugar is lowered by giving phlorhizin (phloridzin), there is an increased drain on the blood sugar and thereby on the glycogen reserve. The author studied the influence of intravenous phlorhizin on 89 children and on 66 adults comprising (1) healthy persons (2) diabetics and (3) patients with various liver diseases. The results show that in conditions in which the glycogen reserve of the liver is adequate the blood sugar remains relatively constant, but if the glycogen reserve is inadequate (as in diabetes mellitus) the blood sugar level drops and ketosis may develop. Diabetic adults do not retain carbohydrate in their livers to the same degree as do normal adults. Removal of relatively small amounts of sugar from their blood results in a further deprivation of liver glycogen with development of hypoglycaemia and ketosis. Children cannot retain carbohydrate to the same degree as adults can because of an increased rate of glycogenolysis. This is true of normal children but even more evident in diabetic children and accounts for their susceptibility to ketosis. The giving of carbohydrate to normal children results in a greater deposition of liver glycogen than it does when given to diabetic children so that the susceptibility of the former to ketosis is decreased. Patients with liver dysfunction have an inadequate glycogen reserve. Phlorhizin may be useful in assessing the severity of diabetes mellitus in a particular patient, since with a given loss of glycogen from the liver, differences in susceptibility to ketosis and in blood sugar fall may be found. Phlorhizin may also be of help to determine the presence or absence of latent diabetes mellitus.

Treatment

Globin zinc insulin.—Lawrence deprecates the premature appearance on the market of globin zinc insulin (G.Z.I.) because it has not received proper clinical trial in Great Britain. If G.Z.I. is proved to be superior to protamine zinc insulin (P.Z.I.), P.Z.I. should be withdrawn to avoid confusion, but neither the encomiums published in America nor Lawrence's own trials have convinced him that the alleged superiority is real. In 6 mild cases under hospital control the patients did not show any appreciable difference in blood and urine tests

when G.Z.I. was substituted for P.Z.I. and parallel findings in a case of severe diabetes mellitus are tabulated. Soluble insulin is strong but is short-lived in action. P.Z.I. is weak and prolonged, therefore large doses involve risk of hypoglycaemia at night. G.Z.I. given as one dose before breakfast, seeks to control sugar by day, to avoid hypoglycaemia at night and still to prevent serious relapse before breakfast next day. An effect so extensive is too much to expect of any one preparation. G.Z.I. is weak and in many cases will require supplementing with soluble insulin as does P.Z.I. In the case of P.Z.I. an excess of protamine complicates the admixture. If G.Z.I. contains an excess of globin a like difficulty will arise. Already errors occur among insulins although P.Z.I. is cloudy and soluble insulin is clear. G.Z.I. being water-clear will make errors all the easier if the only distinguishing mark is a label. Potent drugs should not be marketed except after clinicians have been consulted; administrative machinery for control, if non-existent, should be created.

Soluble insulins and protamine zinc insulin.—Lawrence and Oakley discuss their methods of treating very severe cases of diabetes. They found the most convenient method to be the administration of a mixed dose of soluble insulin and protamine zinc insulin in the morning, before food, given together in the same syringe, the dose of soluble insulin being usually larger than that of P.Z.I. in order to allow for precipitation by the excess protamine present. In very severe cases however this method may fail. Another arrangement is the addition of a small injection of soluble insulin towards the end of the day to prevent the evening relapse. Even so a relapse by the morning may occur. Morning and evening injections of soluble insulin have the merit of simplicity but may fail on account of the tendency to produce a swinging blood sugar, severe hypoglycaemic reactions alternating with intense hyperglycaemia and ketosis. The authors have also obtained favourable results with a morning dose of soluble insulin, which exerts a rapid action after breakfast, and an evening dose of mixed soluble insulin and P.Z.I., which prevents morning ketosis and a high fasting blood sugar. The real danger is nocturnal hypoglycaemia, to avoid which a small dose of P.Z.I. is given.

Factors complicating the treatment of diabetes

Infections

Fungous infection of the brain.—Gregory, Golden and Haymaker point out that prominent among the moulds are members of the class *Phycomycetes*. Of this class the order *Mucorales* contains one family, the *Mucoraceae*, which is parasitic in animals and man. Recorded human infections are scarce, and include but one case of generalized dissemination of the fungus. In most cases there is invasion of lungs or ears alone, but infection of the stomach, nose and skin occurs; only rarely is the central nervous system involved. The authors describe in detail 3 patients who died after *Mucor* infection of the meninges and brain, the fungus having entered through the orbit. All 3 patients had uncontrolled diabetes mellitus. There is a great incidence of fungous infections in diabetics, in conformity with the decreased resistance of diabetics to various infections. The authors did not obtain cultures of the fungus, but the large diameter of the lymphae, the manner of branching and the coenocytic structure were characteristic of the *Mucoraceae*. In 17,400 necropsies at the Johns Hopkins Hospital 10 cases of fungous infection of the central nervous system are recorded. Of these 6 were due to torulosis, 3 to actinomycosis and one to coccidiosis. Only one other well founded case of *Mucor* infection of the central nervous system is recorded. The authors' cases are the only ones in which there was direct invasion of meninges and brain.

Diabetics and daily work

Bishop points out that under present conditions the employment of diabetics in industry must be considered. Diabetics may be so employed provided that their disease is properly controlled and that they are given suitable work. Trauma could directly cause diabetes only when the pancreas was injured to an extraordinary degree (destruction of from three-fourths to nine-tenths). This occurs very rarely. Quick death is the usual result. Diabetes is not produced by shock or emotional strain except perhaps in exophthalmic goitre induced by severe emotional shock. The resultant increased metabolism may however aggravate existing diabetes or bring latent diabetes to notice. Injury to the head or nervous system may be accompanied by glycosuria but does not produce diabetes. Glycosuria often follows injury, but it is transient and diabetes does not result. Injuries which enforce inactivity may, by a great reduction in the utilization of sugar by the muscles, make an existing diabetes worse or make manifest latent disease. Infections do not cause diabetes, but often make existing diabetes worse. With control of infection the diabetic state returns to its previous level. Patients in whom the disease seems to have been brought to light by trauma or infection must be considered to have inherited a constitutionally inferior system of islands of Langerhans. The sulphonamide drugs have no deleterious effect on diabetes and are as potent in the control of infection as they are in non-diabetics. Inhalation anaesthesia may be followed by glycosuria but there is no good evidence to show that it can cause diabetes or make an existing diabetic condition worse. There is no specially deleterious effect from pentothal sodium intravenous anaesthesia, or from pontocaine or novocain used intraspinally. Ether is the general anaesthetic of choice for diabetes. Local anaesthesia for surgery of the extremities should be avoided because of the association of vascular disease with diabetes that is often found; tourniquets may be dangerous for the same reason.

Ahronheim, J. H. (1943) *Amer. J. Path.*, **19**, 873.

Bishop, W. A. (1944) *J. industr. Hyg.*, **26**, 55.

- Gregory, J. E., Golden, A., and Haymaker, W. (1943) *Johns Hopk. Hosp. Bull.*, **73**, 405.
 Hughes, H., Ware, L. L., and Young, F. G. (1944) *Lancet*, **1**, 148.
 Korenberg, M. (1943) *Arch. intern. Med.*, **72**, 746.
 Lawrence, R. D. (1943) *Brit. med. J.*, **2**, 103.
 — and Oakley, W. (1944) *Brit. med. J.*, **1**, 422.
 Nix, N. W. (1943) *Canad. med. Ass. J.*, **49**, 189.

DIAPHRAGM DISEASES

See also B.E.M.P., Vol. III, p. 673.

Subphrenic abscess

Causes

Review of cases occurring in children.—Ladd and Swan review 14 cases of subdiaphragmatic abscess in children. The serious nature of the condition is clearly shown by the fact that 4 of the patients died, one after operation. Eleven were treated surgically. Nine of the children were boys. All but one were of the white race. All were under 11 years of age and 6 were under 2 years. In 9 cases the abscess was secondary to some form of intra-abdominal sepsis: ruptured appendix in 5, primary peritonitis in one, ruptured ileum in one and liver abscess in 2. In one case of a child who had been accidentally run over, the origin was traumatic and appeared after conservative treatment of injury to the liver. In the remaining 4 it was metastatic from a distant focus, including upper respiratory infection in 2, otitis media in one and multiple hordeola in one. The authors suggest that the comparative rarity of subdiaphragmatic abscess in childhood depends upon the fact that the suspensory ligaments of the liver are shorter in children than in adults and tend to hold the liver up against the diaphragm thus keeping the supra-hepatic spaces closed. In the present series the abscesses were localized as follows: right antero-superior in 8; right postero-superior in 3; left superior, right inferior and left antero-inferior, one each. Explanation cannot be offered for the comparatively great incidence of right antero-superior abscesses which conflicts with published figures. Clinically three chief types of picture were seen. (1) A subphrenic abscess which forms part of a widespread intra-abdominal or generalized septic infection. The onset is fairly abrupt with fever accompanied by signs of abdominal involvement such as vomiting, pain, diarrhoea, tenesmus or ileus. Death occurs within a few days. Treatment is unavailing even if a diagnosis is made. (2) An abscess which complicates the course of acute ruptured appendicitis. Persistence of fever and leucocytosis is the most significant sign. (3) A metastatic abscess, the onset of which is insidious, with pyrexia, malaise and gradual development of a mass in the upper abdomen. Drainage, best by the extraperitoneal route, is the only adequate treatment for groups (2) and (3).
 Ladd, W. E., and Swan, H. (1943) *New Engl. J. med.*, **229**, 1.

DIARRHOEA

See also B.E.M.P., Vol. IV, p. 1.

Aetiology and pathology

Diarrhoea associated with organic intestinal disease

Primary inflammatory lesions of the large intestine.—Callender discusses the significance of dysenteries and diarrhoeas when they occur in armies during war-time. Diarrhoeal diseases, especially bacillary dysentery, have in the past been one of the most important causes of non-effectiveness among soldiers and at the present time, also, epidemics are prevalent among troops under field conditions. Diarrhoea may be due to many causes, including malaria, visceral leishmaniasis, avitaminosis and secondary infection in schistosomiasis, but the most significant factor in the causation of diarrhoea is the formation of primary inflammatory lesions of the large intestine. Although *Entamoeba histolytica* causes primary disease of the intestine it is the secondary organisms in the ulcers that cause the symptoms associated with dysentery. The incidence of dysentery from the above protozoon is low however and at the present time in the Forces the chief causal organisms in diarrhoeal conditions are those in the shigella group and in the salmonella, colon and proteus groups. When poor sanitary conditions exist the infecting organisms are always multiple. *E. histolytica* may be found by the examination of fresh stool specimens but the laboratory diagnosis of bacillary dysentery requires skilled workers and specialized methods for the identification of all the infecting organisms. The author points out that examination of the stool for the presence of inflammatory exudate, together with pus and blood, should be made in epidemics of diarrhoeal disease; this would be a simple method of estimating the incidence of cases of bacillary dysentery even if the specific bacteria were not identified in all cases.

Callender, G. R. (1943) *War Med.*, **4**, 459.

DIARRHOEA IN INFANCY AND CHILDHOOD

See also B.E.M.P., Vol. IV, p. 21; Interim Supplement, No. 11*; and Cumulative Supplement, Key No. 308.

Diagnosis and differential diagnosis**Unsuspected mastoiditis**

Association with diarrhoea, vomiting and dehydration.—Unsuspected bilateral purulent mastoiditis is believed by Leathart to be a common cause of diarrhoea, vomiting and dehydration in infants. At this age the Eustachian tube is more horizontal than it is in adults and when the child is lying on his back it offers an easy entrance to milk or to other fluids. Thus it frequently happens that mastoiditis is set up in this way in children who are so young or so ill that they are fed lying down or are allowed to lie on their backs for a long time. In infants none of the ordinary signs of acute mastoiditis are present but the presence of enlarged glands in the posterior triangle of the neck is an almost invariable and highly significant finding. Without operation death is inevitable; with operation 80 per cent of patients recover. The author urges that exploration of both mastoids, an extremely simple operation in infants, should be carried out in all cases of diarrhoea and vomiting which fail to respond to treatment and in which the child is going downhill. It can be done either under light general anaesthesia or if any respiratory infection is present, under local anaesthesia. Not all cases of mastoiditis require operation but if the condition is progressive surgical help must not be withheld.

Treatment**General principles**

Glaser and Bruce, who advocate modifications in treatment of diarrhoeas and dysenteries in new-born infants, consider their patients under the headings of nutritional and dysenteric diarrhoea. For both groups intestinal rest comes first: a period of twelve hours of starvation has been found to be satisfactory. Dehydration was countered by giving plain sterile water at short intervals, supplemented in advanced dehydration or acidosis by intravenous administration, by continuous drip through an ankle-vein cannula, of saline, glucose or Hartman's solutions. Blood transfusion, or plasma if haemoconcentration is high, was valuable later. After twelve hours buttermilk was provided in quantity limited only by the appetite. Of 49 infants 7, intolerant of buttermilk, received skimmed boiled milk and one had protein milk. These diets, to which the diarrhoeic infant is necessarily restricted, contain only half the calorific value of breast milk and of the accepted milk formulas; as the enfeebled infant has increased calorific need, consumption was large but accelerated recovery proved that appetite was a reliable guide to the quantity necessary. During 1938, 1939 and 1940 an average of 16.6 days in hospital was required for recovery, but in 1941 and 1942 only 9.6 days were necessary and the percentage death rate decreased from 27.7 to 12.7. The average length of stay in hospital for patients with Flexner's dysentery who were treated with sulphathiazole was the same as for those who were treated with sulphaguanidine, but the average stay of patients with Sonne dysentery was shorter when they were treated with sulphathiazole than when they were treated with sulphaguanidine. In diarrhoea as distinct from dysentery, the effects of sulphaguanidine medication surpassed those of sulphathiazole; treatment without sulphonamides had still better results. In 14 cases without bacteriological records both drugs proved to be effective, but sulphaguanidine was more effective than was sulphathiazole. A polyvalent antidyenteric serum was used once with great success. Bismuth and paregoric were reserved for resistant cases only.

Glaser, K., and Bruce, J. W. (1944) *J. Pediat.*, **24**, 53.

Leathart, P. W. (1943) *Brit. med. J.*, **2**, 168.

DIETETIC DEFICIENCY DISEASES

See also B.E.M.P., Vol. IV, p. 51.

Prevalence of deficiencies**Deficiencies in Ceylon**

Multiple vitamin deficiency in a prison.—In a paper on the nomenclature of malnutrition Nicholls comments on the variety of symptoms which are caused by a deficient diet. Complications arise from the fact that a poor diet may be deficient in more aspects than one, and by the variability of individual reactions to such deficiencies. In a prison in Ceylon with more than a thousand inmates the diet of curry and rice was the same for all, but whereas some prisoners showed no evident signs of deficiency others had signs of deficiency of one vitamin only—although not the same one in all cases—and some showed signs of more than one deficiency. The incidence of the signs increased after the first month of imprisonment. There were complaints of neuritis, phrynodermia, night-blindness, keratomalacia, sore mouth and scrotal dermatitis. It is reasonable to conclude that all the prisoners suffered from multiple vitamin deficiency. Thirty consecutive cases of malnutrition in children, studied in the Colombo children's hospital, showed a similar variety of signs in skin, mouth and eyes, as well as general symptoms of apathy, irritability and diarrhoea. Since Japan entered the present war there has been in Ceylon a great shortage of rice, which has been replaced by white flour of about 72 per cent extraction and, to a smaller extent, by whole wheat. Thus the poorer children are getting over-milled cereals, eked out with cassava, and very little else. The many names applied to various more or less indistinct types of malnutrition have not aided their accurate comprehension. Nicholls suggests that a more elastic terminology should be adopted, such as the continued use of letters in the naming of vitamins. For example, when

the signs indicated a deficiency of vitamins A and C, or of vitamins D and B₂, they would be referred to respectively as AC deficiency and DB₂ deficiency.

Deficiency of calcium

Diseases due to calcium deficiency

Results of vitamin D therapy.—The effect of vitamin D on young rats maintained on diets lacking in calcium has been investigated by Boyle and Wesson. Twenty-four animals were divided into two groups, one fed on a high protein, the other on a high carbohydrate diet. For each group the phosphorus-calcium ratio was approximately 16:1. Half the number of animals in each group received a daily ration of viosterol (vitamin D). The average gain in weight in the two groups in 12 months was as follows. (1) On high protein diet without added vitamin D, 151 grammes; with added vitamin D, 165 grammes. (2) On high carbohydrate diet without vitamin D, 157 grammes; with vitamin D, 213 grammes. Histological and chemical examination of the teeth at the conclusion of the experiment showed that in both groups addition of vitamin D to the diet brought about pronounced improvement in calcification. In the bones the addition of vitamin D increased the amount of ash and prevented the condition of osteitis fibrosa which occurred in both groups as the result of resorption of bone when the diet was not supplemented. The mortality rates in the 2 groups were as follows. (1) On high protein diet without vitamin D, 33 per cent; with vitamin D, 50 per cent. (2) On high carbohydrate diet without vitamin D, 50 per cent; with vitamin D, 0 per cent. The average retention of calcium was as follows. (1) On high protein diet without vitamin D, 61·2 per cent of the intake; with vitamin D, 50·3 per cent. (2) On high carbohydrate diet without vitamin D, 59·6 per cent; with vitamin D, 75·7 per cent. Thus vitamin D was effective in lowering mortality and in promoting growth and retention of calcium only in animals receiving a high carbohydrate diet but in both groups it considerably improved the structure of the teeth and of the bones. It appears that the influence of vitamin D in promoting calcification of the hard tissues is not to be explained in terms of calcium retention.

Boyle, P. E., and Wesson, L. G. (1943) *Arch. Path.*, **36**, 243.

Nicholls, L. (1944) *Lancet*, **1**, 630.

DIPHTHERIA

See also B.E.M.P., Vol. IV, p. 72; and Cumulative Supplement, Key No. 324.

Bacteriology and pathology

Bacteriology

Selective tellurite medium.—Anderson describes a simple tellurite medium which is highly selective for *Corynebacterium diphtheriae* and which in addition permits a confirmatory microscopical examination to be made. The tellurite medium is made by mixing together potassium tellurite, glycerolated sheep's blood and nutrient agar. The method can be simplified by replacing meat infusion by 'Lab Lemco'. Further, it is possible to combine the tellurite and glycerolated sheep's blood into one mixture and to store it. Cultures from swabs were examined after from 18 to 24 hours' incubation at 37° C. The stains employed were solutions of toluidine blue and of glacial acetic acid, used successively. The tellurite medium is very selective and little growth other than that of *C. diphtheriae* and diphtheroids appear on it. Colonies of *C. diphtheriae* after 18 hours' incubation are from 2 to 4 millimetres in diameter and dark grey in colour and have a metallic sheen. The colony of the mitis type has the appearance of a low dome with a smooth surface and an entire edge and is of a butyrous consistency. The colony of the gravis type is flat, has a mat surface and an irregular edge and displays a 'crust' which cracks when touched with a wire. The intermediate colony has a low dome smaller than the other two, with a coarsely mat surface. The morphological characteristics of *Corynebacterium hafmanni* after 18 hours' incubation are characteristic; the bacilli are short and uniform in size with an unstained central bar and without granules. Of 752 swabs cultivated on the tellurite medium and on Löffler's medium, 212 swabs gave positive results on both media, 119 gave positive results on the tellurite medium only and 15 gave positive results on Löffler's medium only. The medium is suitable for routine diagnostic work, gives more accurate results than does Löffler's medium, is easy to prepare, has stable constituents and suppresses the growth of organisms other than *C. diphtheriae* and diphtheroids. Accurate type differentiation within 24 hours is not however possible. For colony differentiation it is safer to rely on a subculture on rabbit blood agar.

Complications

Circulatory failure

Post-diphtheritic auricular fibrillation.—Campbell, Gibson and Lane report the occurrence of auricular fibrillation during convalescence from diphtheria in a man aged 39 years who was serving in the R.A.F.V.R. The fibrillation lasted for 112 days, when it was stopped by administration of quinidine. The only cardiovascular symptom was palpitation. Multiple peripheral neuritis preceded the fibrillation by 32 days. The patient's parents both suffered from hypertension. He was by profession a dentist; he had never had any rheumatism or chorea and had always been fit. On 6th October 1942, he had a sore throat. He was sent to bed on the 8th, but returned to duty on the 12th. After a few days he cycled 40 miles without undue fatigue. On 19th October his food began to regurgitate through his nose;

otherwise he felt well. He reported sick and was admitted to the Isolation Hospital on 10th November. On 20th November he noticed sudden onset of tachycardia and pulse irregularity, which were considered to be due to extrasystoles. He was ordered complete rest. About this time he noticed tingling of his hands and feet. About 10th December the palatal paresis started to improve and he began to get up. Three throat swabs were negative for *Corynebacterium diphtheriae*. Serum was not given. He went on sick leave on 19th December. Palpitation became conspicuous despite the fact that he was leading a quiet life. There was not any dyspnoea. He noticed an unpleasant tingling in his feet when he was walking. When examined on 23rd February 1943 he was fibrillating, and had hypo-algesia over his soles. Treatment with quinidine, 5 grains thrice daily, was begun in hospital on 5th March, and after he had taken 15 grains his pulse became regular. Teleradiographs of the heart were normal. The blood pressure was 145/95 millimetres Hg. The authors have found only one similar case recorded. Auricular fibrillation in diphtheria may occur in the acute phase or much more rarely as a late single manifestation of myocardial damage.

Diagnosis

Bacteriological confirmation

Limitation of laboratory diagnosis.—It has been reported that in two London County Council hospitals diagnosis could not be confirmed in from 33 to 50 per cent of the cases notified as diphtheria. Wright, by defining the present scope and limitations of the laboratory diagnosis of diphtheria, explains the difficulty of giving an accurate opinion in many cases, even after considerable delay. In the patient's interest a rapid and unequivocal diagnosis is required and in acute, well developed cases the experienced clinician has little difficulty. In milder cases however and in those of contacts and carriers he has to rely largely on laboratory diagnosis. Here the bacteriological difficulty is caused mainly by the different individual and colony forms which *Bacillus diphtheriae* may assume and its close biological relation to the non-toxicogenic diphtheroid bacilli. Direct microscopic examination of the exudate, even in severe cases, is of little value. Culture on Löffler's serum medium is still the method of choice, especially in milder cases. The author points out the anomalies and variations, both macroscopical and microscopical, which may appear in cultures and suggests many ways in which the margin of error in this respect may be reduced. One method, much in use, is to sow cultures on one of the tellurite media—such as Hoyle's modification of Neill's medium—in parallel with cultures on Löffler's serum. Although it promotes the growth of diphtheria bacilli less rapidly than Löffler's does, Hoyle's medium is helpful in identifying young cultures and thus saves time in diagnosis. In many cases in which clinical disease does not exist, such as those of contacts and carriers, or in the investigation of aural and nasal discharges, it is often essential to isolate the suspected organism by plate culture and to test its virility biochemically and by animal inoculation, a procedure which takes at least 5 days.

Prevention

Immunity standards

Antibacterial mechanisms in non-immunized subjects.—In an investigation on the Schick test in young adults, none of whom had been immunized against diphtheria, Goldsworthy and Wilson found that the proportion which reacted was surprisingly large. They say that a similar result has been noted by many other observers. Tests made on poorer people living under unhygienic conditions in a crowded city show that immunity (as revealed by the presence of antibodies detectable by the Schick test) is there acquired early in life. The authors conclude that a failure to react to the Schick test usually indicates effective immunity; a reaction to the test merely points to the fact that in most cases there is only a certain amount of antitoxin in the blood, and it does not tell whether a person has or has not complete immunity. It would seem therefore that there is another protective mechanism which prevents a *Corynebacterium diphtheriae* infection. The Schick test cannot indicate the presence of this antibacterial mechanism. At present complete knowledge of the reaction between *C. diphtheriae* and the human host cannot be obtained if we think of the protective mechanism as referring to antitoxin only. The authors quote Lewis's theory to explain immunity in people who nevertheless react to the Schick test, in which he holds that they may have had a slight infection which has stimulated their defence mechanism without actually producing antitoxin so that they continue to react to the Schick test. When exposed to actual infection their 'primed' mechanism responds quickly and prevents clinical diphtheria.

Immunization

Response to A.P.T. and T.A.F.—A carefully controlled investigation in which the requisite Lf dosage of alum precipitated toxoid has been studied and which yielded information on the problem of dosage balance is described by Bousfield. The results showed that, when sub-optimal or minimal quantities of the toxoid are used, the primary dose should consist of not less than approximately one-half or more than two-thirds of the total Lf units employed. The cause of failure to produce satisfactory immunity is generally a deficiency of the primary stimulus. When minimal amounts of the toxoid are used there is a higher Schick conversion rate if the larger of two unequal doses is given first, which again emphasizes the importance of providing an adequate primary stimulus. It is shown that in the human subject there is no particular difference in the results of injection of concentrated or diluted alum precipitated toxoid if the number of Lf units is the same in each case. The efficiency of a substandard alum precipitated toxoid of 30 Lf per cubic centimetre potency given in 2 injections of 0.5

cubic centimetre has been found highly satisfactory, even one year after the first negative post-immunization Schick test. When adequate total dosage of alum precipitated toxoid is used, the short interval of 14 days between injections may be allowed. The incidence and severity of local reactions after priming doses of 10 Lf and 15 Lf units have been studied. A slightly increased risk of reactions apparently occurs when the larger dose is given, but it is thought that it is not sufficiently great to preclude the use of a standard 0.5 cubic centimetre dose of toxoid with a 30 Lf potency. This dosage should be adequate for all injections, namely primary, secondary, and boosting. Duke and Stott describe a survey of artificial immunity against diphtheria in a country district in which 95 per cent of the child population of 9,600 had been immunized. More than 3,000 children between the ages of 2 and 6 years were Schick-tested after a complete course of immunization. Not one was positive when tested from 3 to 6 months after immunization. The number of treated children who lost their immunity to diphtheria increased steadily as the time interval increased and rose from 4 per cent after 2 years to 18 per cent after 6 years.

Treatment

Antitoxin therapy

The work of O'Meara.—Murray stresses the notable reduction in the fatality rate of diphtheria since the use of antitoxin was introduced. The employment of the Schick test and of active immunization have resulted in a pronounced lessening of the incidence of the disease. Since 1927 there have occurred in Europe several outbreaks of diphtheria which have proved relatively refractory to serum therapy. Of the three strains of *Corynebacterium diphtheriae*—*gravis*, *intermedius* and *mitis*—the association of the *gravis* type with severe and often antitoxin-resistant clinical diphtheria is established. Such cases are characterized by severe toxæmia, by oedema of the cervical tissues which leads to 'bull-neck', by a great incidence of paralysis and by a greater case fatality than that found in association with the other varieties of *C. diphtheriae*. Moreover there is a tendency for clinical diphtheria to develop in Schick negative persons and even in subjects who have been previously actively immunized; the *intermedius* and *mitis* varieties have been found in association with the latter subjects but in a much smaller proportion of cases. In areas in which the *gravis* strain is the predominant variety hypertoxic diphtheria is recorded, but in localities in which *gravis* is of infrequent occurrence a particularly severe clinical case does not necessarily appear as a result of infection, nor does serum resistance prevail. Liverpool proved an exception to the rule in that, although the *gravis* type accounted for 70 per cent of the cases in 1940, the greatest case fatality rate was associated with the intermediate type. Murray refers to the researches of O'Meara who in 1940 demonstrated that the diphtheria organism produced two components in its toxin. One of these, substance A, is the toxic component characteristic of Park-Williams 8 strain which is commonly used for commercial antitoxin production. The other component, substance B, O'Meara considered to be of the nature of a diffusing factor. He suggested that commercial antitoxin is rich in antibody A but poor in antibody B. *Gravis* organisms in his hands produced a large proportion of substance B and hence are hypertoxic and serum-resistant. Clinical reports of the success of serum rich in substance B have supported O'Meara's contention. It is not yet possible to produce such an antitoxin at will since the factors governing its production have not as yet been determined. There is not available definite evidence to show why *gravis* infection has increased within recent years. Murray states that the *mitis* strain predominates in South Africa and that a large proportion of Schick positive reactors exists in this area. Contact with South African troops returning from Egypt is a source of danger since there has been a large proportion of *gravis* types in diphtheria contracted there. Murray advocates the immunization of as large a proportion of the European population of South Africa as possible, particularly in the 1–10 years age group; observation on the bacteriological types of *C. diphtheriae* occurring in the Union should be continued.

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DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS AND ASSOCIATED INJURIES

See also B.E.M.P., Vol. IV, p. 113; and Cumulative Supplement, Key Nos. 326-353.

Treatment

General principles

In his presidential address to the British Orthopaedic Association Girdlestone discusses the treatment and especially the maltreatment of fractures. Many cases are treated by men who have little or no interest in fractures and who do not grasp the principles involved. The remedy advocated is twofold, first that the best man available in each district should be chosen by the doctors in the district for the primary care of fractures and secondly that all difficult fractures

should be transferred to the hands of experts. The three aims of treatment are (1) freedom from pain, (2) freedom from pins (wherever possible) and (3) freedom of circulation. Powerful persistent weight and pulley traction is harmful and delays healing. Fixed traction such as is provided for fractures of the femur by the Thomas-Pearson-Balkan frame combination is preferable. Great restraint should be exercised in the performance of elaborate operations. The simplest method of attaining a good result is the one to be preferred.

Union

Discussion of modern treatment methods.—A reaction which favoured early movement of fractures, almost to the point of danger to their reduction, succeeded the established ideal of absolute and prolonged immobility. Burns and Young deprecate the current return to absolute immobility and support the dictum that 'bone and soft-part treatment are of equal importance and often should be simultaneously undertaken'. Prolonged immobilization threatens the elderly with permanent stiffness and younger patients regain free movement only after protracted treatment or may often regain only restricted movement. A fracture of the tibial shaft which is immobilized in plaster may involve the subastragalar, tarsal, metatarsal and even the phalangeal joints. Moreover, the circulation becomes reliant on the plaster support and requires a subsequent semi-rigid dressing for two months to restore vascular tone. Fractures are divisible into three groups. (1) There are the readily uniting fractures of the ribs, clavicle, femur and digits, oblique fractures of the humerus and fractures of cancellous bone. Here firm fixation is unnecessary and treatment should be concentrated, with much reduced splinting, on early movement. Thus a patient with a fractured femur which has been subjected to extension can move the knee, and a spiral fracture of the humerus supported on a U-shaped slat allows movements of shoulder and elbow. (2) The fractures which unite with difficulty include those of the femoral neck, and transverse fractures of the tibia, radius, ulna and humerus. Here internal fixation, which allows immediate joint movement, is better than plaster splinting. (3) In fractures which involve joints, if there is no deformity, fixation is unnecessary. Deformities which must be accepted as irremediable do not benefit from fixation and the cancellous bone implicated readily unites. Fixation is desirable only when reduction of displacement is both possible and necessary.

Regional

Shoulder joint

Habitual dislocation of the shoulder.—Henderson reports on a new technique for the cure of habitual dislocation of the shoulder, of the type in which the head of the humerus emerges through the weak antero-inferior portion of the capsule and ascends to rest beneath the coracoid process. After appropriate skin incisions, one hole is drilled through the tip of the acromion process and another through the head of the humerus, outside the joint capsule. The peroneus longus tendon in the leg is then exposed and half its diameter is excised from about 6 to 8 inches of its length. This strip of tendon is threaded through the bony canals already prepared and its ends are overlapped and sewn together. The suspensory ligaments thus formed should be deeply placed and under a fair amount of tension. No abduction of the arm is allowed for 14 days. Thereafter a movement of 20–25° is permitted. Right-angle abduction is forbidden until 3 months after operation. Fifty-five of these so-called 'teno-suspension' operations were performed on patients whose ages varied from 16 to 50 years. Outdoor games and sports or a fall accounted, in most cases, for the primary dislocation. Successful results with unrestricted movement of the joint were recorded in 91 per cent of cases after a lapse of time varying from 15 months to 19 years. Interference with the function of the peroneus tendon was neither noted nor complained of. Of the 5 failures, 3 occurred in epileptic patients and the remaining 2 were probably due to faulty technique. It is claimed that this operation, which is simple and shows a high percentage of permanent cures, has definite advantages over other methods in which slings are devised from the tendons of adjacent muscles or from strips of fascia lata or in which the glenoid cavity is made deeper by a bone graft.

Fractures of femur

Bone grafting.—Eleven cases of fracture of the femur seen within a month of occurrence and 9 in which treatment had been given for a period exceeding two months and which required revision are considered by Peterson. Failures result from incomplete immobilization, from premature or vigorous movement and from unsupported bearing of weight. A walking brace is essential until union is firm. Immobilization in plaster is suitable for transportation only. As a sole treatment it permits over-riding and as an adjuvant after operation it inhibits the recovery of knee movement. Suspension traction is simple, safe and often adequate, if the results are checked by repeated radiograms and if the nursing is skilled. Distraction from excessive extension and overlapping from insufficient extension are the disadvantages peculiar to the method. Single pins are inadequate in reduction; the dual pin method should be reserved for recent single fractures of the shaft as it is unsuited for use in fractures near joints, in fractures of long standing and in fractures with a large free displaced fragment. Reduction by open operation, the earlier the better, is excellent but success depends upon the size of screws and plates being adequate. Screws should traverse the cortex on both sides. The preservation of a sufficient blood supply and the danger of infection are the obstacles to be surmounted. Bone grafting is required for non-union. The graft, 6 inches long, includes periosteum, cortex and medulla and is supplemented by free use of chips and medullary

bone. From the recipient femur sufficient cortex is removed to make a flat surface and the medulla is exposed for the full length of the graft. Long screws are employed, usually with a plate, which permits earlier knee movement. The results of this treatment were highly satisfactory.

Fixation by screw.—Johnston, emphasizing the importance of as short a period of confinement to bed as possible for elderly patients with fractures of the femoral neck, describes a method of screw fixation in such cases by means of a combination of screw and nail. The screw offers more security than does the nail in holding the parts together and the use of the hammer is unnecessary. The screw should penetrate the head of the femur as far as possible and the threads of the screw should not extend below the line of fracture. The length of the screw is determined by the measurement of the distance from the outer cortex of the shaft to the outer cortex of the head; the X-ray film of the opposite hip is used. If the screw inserted should prove to be of incorrect length it may be removed and a fresh one be inserted. The use of the fluoroscope in the fixation of hip fractures is essential. Under spinal anaesthesia the fracture is reduced; the leg and foot are brought over the edge of the table at a right angle to the thigh and placed in a leg holder which maintains the leg at 18° of abduction. If the X-ray examination shows satisfactory reduction, a heavy wire is placed on the patient's hip under the screen and manipulated as a guide to the direction of insertion of the screw. A guide wire is inserted through an incision in the skin and if skiagrams show a satisfactory position, the screw is placed upon the guide wire and driven into place, again under control of fluoroscopy. The author finds that the method is simple and causes very slight shock to the patient.

Fractures of shafts of tibia and fibula

Ice-skater's fracture.—A type of fatigue fracture referred to as 'ice-skater's fracture' is described by Ingersoll and 3 cases are reported. Fatigue fractures are relatively asymptomatic and occur in apparently normal bone without displacement of the fragments. They are caused by repeated trauma and occur at the area of maximum bending. Muscle, tendon and bone fatigue appears to be a predisposing factor. Ice-skater's fracture occurs in the lower end of the shaft of the fibula. In the cases recorded each of the patients was a 9-year-old boy: in one case the fracture was bilateral. In skating the skate exerts an inverting or everting leverage on the foot; considerable external rotatory force is exerted on the ankle while the foot is kept fixed on the ice and eversion is a prominent factor. The less efficient the skater the greater is the degree of eversion maintained. The mechanics of the ankle joint are discussed in relation to the stresses to which the foot and ankle may be subjected. From analyses of the forces in play when the foot is in eversion it is seen that the weight-bearing line shifts laterally and increases the pressure on the external (lateral) malleolus. There is also a torsion strain due to external rotation. Two main types of fracture occur during eversion with external rotation. Both malleoli may be fractured or the fibula may break near the distal end, usually about 2 or 3 inches from the tip, in its thinnest part. In the author's cases the diagnosis was made radiologically. There was not a history of injury and the patients complained of pain, limping, and slight swelling over the outer side of the leg above the ankle. In the case with bilateral fractures congenital syphilis was suspected; the possibility of traumatic periostitis, non-pyogenic osteomyelitis or primary bone tumour was also considered but the diagnosis was confirmed later when the two cases of unilateral ice-skater's fracture were seen and the similarity of the lesions was noted.

Treatment by use of the sliding graft.—Burns and Michaelis describe the technique of the use of the sliding graft in the treatment of ununited fractures of the tibia and the results they obtained. A long skin incision is made about half an inch lateral to the anterior border of the shaft. After the periosteum has been stripped, a 5–6 inch graft is cut in the bone above the level of the fracture, and half that length of bone is removed from the tibia below the fracture line. The graft can be slid down as far as is necessary and when it is in place the alignment of bone will be correct. When the fracture is low down the graft has to be sunk fairly deeply into the cancellous bone in order to restore the normal varus curve. The saw cuts are made sloping slightly together from before backwards. The small lower piece of bone may be used to reinforce the main graft at the fracture or to fill in the space left by the sliding down of the main graft. The graft, once in position, is fixed by the insertion of from 4 to 6 vitalium screws. A well padded plaster is applied from the groin to the toes and left on for 14 days. The age of the patients, and the duration of the fracture, were very varied; 15 compound fractures were included. If the latter were infected, operation was postponed until 3 months after cessation of discharge. Of the 26 fractures in the series, 21 were united in 3–4 months, 3 at 5 months and one at 7 months; one failed to unite.

Ankle joint

Sprains.—Five hundred cases of ankle sprain of all degrees are reported by McMaster. The patients were mostly in active military service but older men and 8 women are included. Fractures were eliminated by routine radiography. The anterior talo-fibular ligament alone or with other ligaments was affected in 90 per cent of cases. Points tender to palpation defined the ligament injured. The injection of procaine hydrochloride (novocain) was employed for over 200 patients, over 200 were strapped with adhesive tape and 28 were treated by the application of an elastic bandage only. Cold succeeded by hot applications were employed for 22 patients and 18 were dismissed untreated. Two per cent procaine without

epinephrine (adrenaline) was used in amounts of from 10 to 20 cubic centimetres but this amount can be freely exceeded. Enough was injected with a small needle into the disinfected skin to raise a weal. The ligament was then injected through a larger needle until all tenderness on movement or to palpation was abolished. Next an elastic bandage was adjusted which was removed and rewrapped in an hour's time in order to avoid constriction. If any pain was experienced when the patient walked the injection was repeated; he was then allowed to return to activity except that he was forbidden to run or jump. When sitting he had to keep the ankle moving constantly and he had to report daily. In these cases treatment by injection gives the best results, but irrespective of the treatment employed the ambulatory patient improves more rapidly than the resting patient, who may be disabled for weeks.

Foot

Stress fracture.—According to Hartley, fatigue (or stress) fractures of bone appear to be very little known in Great Britain. It is true that 'march foot' has become widely recognized and much reported since 1855, when Breithaupt was apparently the first to describe it, but until 1939 there does not appear to have been any recorded case in Great Britain of stress fracture except in the feet. There is obviously a curiously low incidence rate of this form of fracture both in America and in Great Britain. In Germany a single author, Sheller, recorded 590 cases in 1939. The introduction of conscription or the preparation of the nation for war appears to be followed by a large increase in the incidence rate of stress fractures. This is indicated by the selection of the term, soldier's fracture, in the description of 4 examples by Nordentoft in Norway. It is possible that bone exhaustion findings may prove to be relatively common when adequately sought for, just as has the developmental anomaly known as craniolacunia, hitherto believed to be rare in Great Britain but now known to occur in 0.94 per cent of the population. Stress fractures are commonest in the years of adolescence and early manhood; the youngest patient in the author's cases was 7 years of age. Callus is a prominent feature. The bones affected are the long, weight-bearing or heavily stressed—femur, tibia, fibula, metatarsals and tarsals. There is not any evidence of a convincing character of a causal disease. The author's view is that pseudo-fractures are distinct from stress fractures in that they always occur in pathological bone. The importance of early diagnosis in mild cases without mobilization is insisted upon. Differential diagnosis must be made from the following groups or conditions. (1) Pathological fractures in congenital defects, general systemic disease, and metastases and tumours of bone; (2) *Umbauzonen* (Looser's 'transformation zones') or pseudo-fractures in osteitis deformans, osteomalacia, rickets; (3) primary malignant disease of bone, sarcoma, Ewing's tumour; (4) tuberculosis, syphilis, low-grade haematogenous osteo-periostitis; (5) simple fractures due to trauma; (6) osteomyelitis.

Spondylolisthesis

The lumbo-sacral articulation.—Prespondylolisthesis, according to Galluccio, connotes a defect unilateral or bilateral of the pars interarticularis of a vertebral neural arch. Spondylolisthesis is the displacement of the vertebral column, usually forward, and results from such defect subject to trauma or occasionally from trauma alone. The condition is most frequently seen in males during the third and fourth decades and in 80 per cent of cases affects the lumbo-sacral articulation. The stability of this articulation is promoted when the articulation of the inferior articular processes of the fifth lumbar vertebra with the superior articular processes of the first sacral segment lies bilaterally in a coronal-oblique plane, and the normal lumbo-sacral angle of 42–45° exists. Conversely such articulation tending towards the sagittal plane with exaggeration of the lumbo-sacral angle unstabilizes the lumbo-sacral articulation and throws strain on the pars interarticularis. The cause of the defect in the pars interarticularis, whether it be a congenital defect of ossification or traumatic, is undetermined. Symptoms in spondylolisthesis may be absent. The backache, stiffness and fatigue usually present do not suffice for diagnosis, which is essentially radiological. The antero-posterior, right and left oblique views, to illustrate the 'bow-tie' areas, and the true lateral views are indispensable. Fracture dislocations, Pott's disease, neoplasm, congenital dislocation of the hip and osteomalacia may occasionally require consideration in differential diagnosis. In treatment frequent physiotherapy, postural exercises to reduce lordosis, use of a firm bed and the support of a belt relieve symptoms in one-third of the number of cases. Spine fusion was practised in 2 cases. In 4 of the 15 cases described, the lesions were incidentally detected in films taken for other purposes and symptoms were absent. A history of accident was obtainable in 7 cases. Reverse spondylolisthesis was twice encountered.

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— and Young, R. H. (1944) *Lancet*, 1, 723.

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DISSEMINATED SCLEROSIS

See also B.E.M.P., Vol. IV, p. 187.

Course and prognosis*Classification of types*

Use of individual life chart.—In an article on the prognosis of multiple sclerosis McIntyre and McIntyre describe a graphic form of life chart made by them for 55 patients with this illness. By the use of this chart the clinical problem of multiple sclerosis can be readily grasped. In the chart the duration of an attack is represented by shaded and the remissions by blank spaces; the symptoms of the attack are recorded under the shaded areas. The remissions are graded as I, II and III according to the freedom or otherwise of the patient from neurological disability. In a study of the clinical material 3 forms are recognizable: (1) the remittent, (2) the chronic progressive and (3) the acute type, which is rapid and fatal. One patient in the cases recorded showed clinical symptoms of Devic's disease and remissions resembling those of disseminated sclerosis. The ultimate prognosis for all types is unfavourable although Bramwell considers that in rare instances the patient may recover completely. Prognosis with regard to life is good for the remittent and for the chronic progressive types; patients with the former may be able to lead useful lives for many years. Cases belonging to the acute form of the disease usually terminate fatally within from 7 to 18 months. The prognosis of optic neuritis and retrobulbar optic neuritis is good for the individual attack, only one patient in the series becoming totally blind. No form of treatment is apparently of any value, the life charts of all the 55 patients whether treated or untreated showing similar progress of the disease over the years.

McIntyre, H. D., and McIntyre, Aurelia P. (1943) *Arch. Neurol. Psychiat.*, Chicago, 50, 431.

DIVERTICULOSIS AND DIVERTICULITIS

See also B.E.M.P., Vol. IV, p. 207; and Cumulative Supplement, Key No. 355.

Stages*Diverticulitis*

Clinical picture and treatment.—Young and Young analyse 84 cases of diverticulitis of the colon. Diverticulosis—a prerequisite of diverticulitis—is a hernia of the mucosa through a defect in the muscular layer, which empties readily until irritation causes obstructive oedema of the neck. Then inflammation spreads, causing spasticity and tenderness of the adjacent bowel; this condition constitutes diverticulitis. Perforation with peritonitis ensues, or pericolicitis which either subsides, or infiltrates the bowel with fibrous tissue which causes obstruction, or leads to localized abscess. The abscess may subside or may perforate the peritoneum, the retroperitoneal tissues, the viscera or the abdominal wall. The classical picture shows pain in the left lower abdominal quadrant, slight fever and leucocytosis and flatulence with nausea. Actually, manifestations are protean, and aberrant pain, alternating constipation and diarrhoea, and haemorrhage may be associated. Haemorrhage may be occult or, as in 26 per cent of the series of cases described, visible. Examination by palpation is usually uninformative. From sigmoidoscopy alone a correct diagnosis has been made by Jackman and Pumphrey in 66 per cent of cases. By its means, spasm, hypermotility with obstruction, immobility, angulation, mucosal oedema and occasionally diverticular openings were discovered. Radiography with the barium enema which was used by one worker was a diagnostic success in 90 per cent of his cases, but the differentiation of diverticulitis and diverticulosis offers difficulties, as does the differentiation of diverticulitis and carcinoma in obstructive cases. In treatment, especially of acute diverticulitis, rectal instillations of barium are a valuable adjunct to rest in bed, application of local heat, and administration of mineral oil and sedatives. Intake should be properly controlled. After the giving of a cleansing enema, 30 grammes of X-ray barium in 90 cubic centimetres of warm water should be instilled rectally twice a week until the diverticulitis subsides, and thereafter once weekly as long as the patient will submit to the procedure. Barium given orally may be employed with the same timing. Five indications for the use of surgery—perforation, obstruction, fistula, localized abscess and suspected cancer—bring about 22 per cent of patients to operation. Since resection carries a mortality of 21 per cent the simplest possible procedures, whereby mortality has been reduced to 11·8 per cent, are to be preferred.

Young, E. L., and Young, E. L., III (1944) *New Engl. J. Med.*, 230, 33.

DROWNING: RESUSCITATION

See also B.E.M.P., Vol. IV, p. 233; and Cumulative Supplement, Key Nos. 357 and 358.

Resuscitation*Artificial respiration*

Survey of methods.—Ross describes the findings of the first three years of a survey made in order to assess the efficacy of methods of artificial respiration. The corporations collaborating are the United States Coast Guard, advocating the Howard-Sylvester method, the Fire Departments of Los Angeles and Chicago, employing mechanical devices, and the

Chicago Health Department. Other sources contribute 3 cases to the total of 2,142. Schäfer's method is widely employed. The mechanical devices used are the E and J resuscitator, the E and J inhalator and the H and H inhalator. Mouth to mouth breathing and the Draiger pulmotor receive mention. The information is given in tabular form from which it emerges that neither Schäfer's method nor the mechanical devices employed were productive of injury; that the outlook in cardiac cases is bad and that in all cases treatment started after 15 minutes of apnoea failed. Assessment of comparative values is not yet possible.

Ross, B. D. (1943) *J. Amer. med. Ass.*, **122**, 660.

DWARFISM AND INFANTILISM

See also B.E.M.P., Vol. IV, p. 277; and Cumulative Supplement, Key No. 362.

Pathology and classification

Dwarfism and infantilism

Renal dwarfism and diabetes insipidus.—A case of renal dwarfism associated with diabetes insipidus, in a boy aged 5½ years, is recorded by Mochlig. The important clinical features were dwarfism, disordered kidney function with albuminuria, diabetes insipidus, progressive genu valgum, sexual infantilism and normal intelligence. At the age of one year it was noticed that the child was not growing normally and that dentition was retarded. He drank large quantities of water and craved for lemons. It is probable that there was a hereditary factor in the case as many of the maternal relations were very short in stature. The father was tall and obese and thus there was a duoparental pituitary disturbance. There were 2 other normal children living; the eldest child had died in infancy of pyloric stenosis. The child with renal rickets had extensive hydrocephalus and a primary defect of the pituitary gland as shown by radiological examination; the defect induced a secondary genito-urinary disturbance. Treatment by thyroid medication at the age of one year caused increased growth and enlargement of the carpal bones. Treatment with anterior pituitary extract was given from the age of 2 years. When the patient was 5 years old pellets of testosterone propionate were implanted for the purpose of stimulating osseous development. There was subsequent enlargement of the penis and a temporary growth of pubic hair. The giving of posterior pituitary lobe extract reduced the intake and excretion of fluids to about half the original levels. It is thought that the increase in growth was due to the administration of thyroid extract and not to that of the sex hormone; in fact, the dosage of the latter may have been sufficient to depress the pituitary gland and thus to have aggravated the dyspituitarism. The prognosis in such cases is poor owing to the defective renal development with superimposed nephritis. In the author's case the craving for lemons indicated that the administration of citrates might compensate for the increased excretion of bases. In 1942 the child died at the age of 7½ with signs and symptoms of uraemia.

Mochlig, R. C. (1943) *Amer. J. Roentgenol.*, **50**, 582.

DYSENTERY, BACILLARY

See also B.E.M.P., Vol. IV, p. 317; Interim Supplement, No. 14*; and Cumulative Supplement, Key No. 364.

Aetiology

Water supply

Sonne dysentery arising from water.—The rarity of water-borne epidemics of Sonne dysentery has led Green and Macleod to publish an account of one which occurred in a Somerset town in July 1942. The first case was that of a child in whom, after an operation for supposed appendicitis, diarrhoea developed. This case drew attention to 10 others in children attending a small private school. Within a week the epidemic was in full swing, people of both sexes in all parts of the town falling victims. The total number of cases was never known, since doctors were called only to children and old people, but it was estimated that during the first month nearly 400 people were affected out of a population of 10,000. *Bacillus dysenteriae* of Sonne type was isolated from the stools of the first 6 patients examined. The clinical features were as follows: sudden onset with fever, vomiting and diarrhoea; profuse, watery stools containing blood and mucus; subsidence of fever within a week. Sonne bacilli were isolated from one sample of tap water. The water supply was shared by a village in which no cases of dysentery occurred, and the water had been chloraminated for several years. The water supplied to the village was stored in a separate reservoir in which it remained in contact with chloramine for four days. The results of experiments which were carried out suggested that the concentration of chloramine employed was too low to sterilize the water during the shortest possible period of contact. The amount was therefore increased and the epidemic ceased.

Bacteriology of the dysentery group of bacilli

Analysis of 251 cases

The paracolon group.—Adams and Atwood conducted an analysis of 251 cases of bacillary dysentery which occurred in an army camp. In 90 per cent of the cases organisms belonging to the shigella group were isolated on stool culture; of the organisms, 78·7 per cent were identified as *Shigella paradysenteriae*, 10·2 per cent as *Shigella dysenteriae sonnei*, 8·9 per cent

as *Shigella newcastlei* and 2·2 per cent as *Shigella alkalescens*. A member of the salmonella group was isolated in 6 cases and paracolon organisms in 33 instances. The authors required identification of a pathogenic organism for the diagnosis of bacillary dysentery. Diarrhoea and gastro-enteritis were present in 750 other cases of illness and it seems likely, according to the writers, that many of these represented cases of bacillary dysentery. The paracolon group presents a relatively new problem and further work is essential in order to ascertain its significance and the methods for its identification. Therapy with sulphonamide compounds was of value against *Shigella paradysenteriae* infections, but the response of *S. newcastlei* was debatable. Infections by *S. sonnei*, *S. alkalescens*, salmonella and paracolon organisms apparently did not respond to therapy.

Treatment

Prophylaxis

Treatment of carriers with succinylsulphathiazole (sulphasuxidine).—Barker records observations on the minimal effective dose of succinylsulphathiazole (2-(*p*-succinyl-aminobenzene-sulphonamido)-thiazole) in the treatment of carriers of bacillary dysentery. Other workers have reported favourable results from oral administration of the drug in daily doses ranging from 0·25 gramme to 1 gramme per kilogram of body weight, the periods of administration ranging between 2 and 17 days. It has been noted that patients who received smaller doses responded better than those who took larger doses, and successful prophylaxis has been obtained by the use of sulphaguanidine (*p*-aminobenzenesulphonylguanidine monohydrate) in doses of 0·5 gramme given orally 3 times daily. Five dysentery carriers were detected among a group of hospital workers handling food. Three of them were treated with 3 grammes of succinylsulphathiazole given 4 times daily for 7 days; the dysentery organisms, however, were still found to be present in the stools at the end of this period. Another course of treatment was given consisting of the same dosage for a period of 14 successive days; the stool cultures were then found to be negative. The fourth patient gave positive stool cultures after taking 3 grammes of succinylsulphathiazole 4 times daily for 14 days, but after 4·5 grammes 4 times daily for a further 5 days had been taken the cultures became negative. The fifth patient however yielded negative results before any treatment had been given and after 2 positive stool cultures had been obtained. In each of the first 4 cases the organisms disappeared from the stools for a few days after the first ineffective course of treatment, but recurred later, and stool cultures should therefore be made for at least 3 weeks after the cessation of therapy. Although comparatively small doses of succinylsulphathiazole will cure dysentery carriers if treatment is continued for a sufficiently long time, it is suggested that in most cases 0·25 gramme daily in divided doses for a period of from 5 to 7 days is for practical purposes the most satisfactory scheme of treatment.

Relative value of the sulphonamides.—Stanier and Stapleton suggest that if the sulphonamides are being used as a prophylactic rather than a curative measure in bacillary dysentery, a high concentration in the intestinal contents should be aimed at. In intestinal infections the organisms are probably confined to the lumen of the bowel rather than present in the mucosa. A sulphonamide preparation which was poorly absorbed would be effective because of its high concentration in the faeces. In observations on patients in a children's ward the authors found that in those receiving either sulphaguanidine or sulphathiazole as a prophylactic against Sonne dysentery, approximately equal portions were excreted in the urine. Urinary output must be maintained when giving these drugs and with sulphathiazole medication the urine must be kept alkaline. After the administration of sulphathiazole the blood levels are slightly higher than after that of sulphaguanidine. Only a very small proportion of succinylsulphathiazole, which was used for 5 patients, was excreted in the urine. The authors suggest therefore that its value is greater as a prophylactic.

General treatment

Sulphaguanidine.—Smith describes the success and limitation of the giving of large doses of sulphaguanidine in treating dysentery of Flexner type. Forty-four young women, of whom 10 were diarrhoeic and 34 were symptomless carriers, each received orally 142 grammes during a period of 10 days. Beginning at 24 grammes given daily for 3 days the dose was progressively diminished. Daily estimations of the blood level of sulphaguanidine corresponded closely with the intake. During a fortnight after the end of the treatment cultivation of 3 successive rectal swabs and 2 faecal specimens from each patient showed freedom from the *Bacillus dysenteriae* of Flexner. In twenty-one patients toxic rashes developed about the ninth day of treatment. The drug was discontinued but such patients had received at least 129 grammes. Ten were generalized morbilliform rashes and the remainder were localized. All rashes faded within 4 days without constitutional symptoms except for slight pyrexia and suffusion in 2 instances. The rashes were not correlated to a high concentration of sulphaguanidine in the blood. For the purpose of testing hypersensitivity 12 of these patients in groups of 3 were subjected to test doses of sulphanilamide, sulphathiazole, sulphadiazine and sulphaguanidine. Eight displayed a toxic reaction to sulphaguanidine but none reacted to the other sulphonamides. The giving of massive doses of sulphaguanidine was successful but the toxic effect, which is apparently contained in the guanidine radical, suggests that the total dose should be limited to 110 grammes.

An experience of 18 months, including two summers, in the Middle East, during which they have treated 1,829 patients who had bacillary dysentery, enables Bulmer and Priest to assess

with some confidence the value of chemotherapy in the treatment of this disease. They have abandoned the use of purgatives and the standard treatment has been rest in bed, plenty of fluids and sedatives for pain. Four hundred and eighty-three patients with non-amoebic diarrhoea, in most cases due to bacillary dysentery, were treated in addition with sulphonamide drugs. Sulphaguanidine was given to 323 patients. The average stay in hospital was materially reduced in this group: in 205 acute cases in which the patients were treated with sulphaguanidine the average stay was 17 days whereas in 600 similar patients chosen at random from the admission book and including some treated with sulphaguanidine the average stay was 20 days. The drug was given in large doses, the average dose being 100 grammes, the maximum 350 grammes. It appears to be almost non-toxic. Very few of the patients were upset by it and the only serious complication was the setting up of renal damage in one case, which cleared up. In 95 per cent of patients recovery was rapid and complete. The authors strongly recommend the routine employment of sulphaguanidine in the treatment of bacillary dysentery. Ninety-seven patients were treated with sulphapyridine. Renal complications developed in one but the patient recovered; malaise, nausea and vomiting were common. The results were not as good as were those obtained with sulphaguanidine. Sulphanilamide was used in 63 cases when supplies of sulphaguanidine were short. It appeared to be of little, if any, value. The average stay in hospital was not reduced. Because of the comparatively high toxicity of both sulphanilamide and sulphapyridine the doses given were much smaller than were those of sulphaguanidine and averaged 20 grammes.

Aperients, sulphaguanidine and chalk mixture compared.—In 200 confirmed cases of bacillary dysentery Jamieson, Brodie and Stiven adopted three treatments: administration of (1) aperients, (2) sulphaguanidine and (3) chalk mixture. In all groups abundant fluid was given and no special diet. Clinical cure was shown by mucus-free stools of normal consistency. In this respect sulphaguanidine gave better results than did aperients. In Sonne III infections, sulphaguanidine gave better results than did the chalk treatment, whereas in Flexner and Newcastle infections, the results of the chalk and the sulphaguanidine treatments were about equal. The type of infecting organism did not materially alter the duration of symptoms in the group which was given sulphaguanidine. The authors stress, in view of their bacteriological findings, the necessity for great care in the handling of faeces from convalescent cases. Thirty per cent of convalescents on sulphaguanidine treatment were bacteriologically positive and 50 per cent of those on aperients or on chalk. The results show that sulphaguanidine is the best treatment in bacillary dysentery. The effect of sulphaguanidine is not much influenced by pyrexia. The drug seems to act better in the acute type of case. In 5 cases of chronic bacillary dysentery no improvement was shown after full courses of sulphaguanidine had been given.

Effect of succinylsulphathiazole on the carrier rate.—An outbreak of dysentery in a military camp is reported by Roberts and Daniels. The disease was in most cases fairly severe but of short duration; as a rule fever lasted for 2 or 3 days and diarrhoea for about 4 days after the patient was admitted to hospital. *Shigella paradysenteriae* Boyd-88 was isolated from 36 per cent of the patients. Cultures were at first made from the stools but the rectal swab method was soon adopted as it was found to give a much higher percentage of positive results. At first all patients received symptomatic treatment. The later cases were divided into 2 groups: (1) consisting of 136 patients who were treated purely symptomatically and (2) a group of 89 who were given succinylsulphathiazole in daily doses of 0.25 gramme per kilogram of body weight, continued until symptoms had ceased for 2 days. The average duration of fever was 2.2 days in the treated and 2.8 days in the untreated patients; the duration of diarrhoea was 7.2 and 7.4 days respectively. There was not any significant difference observed in the severity of the symptoms. The incidence of positive cultures made subsequently was strikingly reduced: of bacteriologically proved cases those patients treated with succinylsulphathiazole showed a carrier rate of 2.6 per cent, compared with 18.2 per cent in a comparable untreated group.

Therapeutic serums and vaccines

Bacteriophage.—The applicability of bacteriophage to bacillary dysentery is criticized by Boyd and Portnoy. Two Army camps in the Middle East unwittingly provided evidence. To the camp for enemy male civilians visitors came, bringing gifts including locally produced bacteriophage, yet admissions to hospital for dysentery were 19.9 per 1,000 during 4 summer months. At the prisoners of war camp, identically circumstanced, simultaneous admissions were 8.6 per 1,000 only, although bacteriophage was unknown. Bayer's *Ruhr-Bakteriophagen Polyvalent*, 'Behringwerke', large quantities of which had been captured during the Axis retreat from El Alamein, was used in the planned investigation of the agent's prophylactic value, of its efficiency in aborting early dysentery or modifying established disease and of certain of its laboratory aspects. The preparation was highly potent against stock cultures of dysentery and typhoid-paratyphoid bacilli and *Bacillus coli*, surpassing French and Alexandrian preparations which were tested simultaneously, and it was similarly potent against organisms isolated from patients. It passed through the bowel unaffected. Clinical experiments which lasted for 2 months divided a camp of German prisoners into a small group for prophylactic studies and two main groups. Immediately on the appearance of diarrhoea patients from one main group received during 3 days 120 cubic centimetres of bacteriophage and patients from the other, sodium sulphate treatment. The percentage in both groups

which required subsequent admission to hospital was practically equal; thus bacteriophage was proved to be ineffective in aborting dysentery. According to the records the bacteriophage group showed slightly milder symptoms on admission, parity in attaining freedom from blood and mucus and 3 days' less detention in hospital than did the control group. In prophylaxis the experimental group before they were treated showed a dysentery rate of 27.5 per 1,000 during one month. After administration of 10 cubic centimetres of bacteriophage on 3 successive mornings the rate fell to 19.5 during the ensuing month; it still exceeded the 10.2 per 1,000 of the control group. This result, coupled with the prevailing low incidence of dysentery, allows only general conclusions to be drawn. Since dysentery bacilli survive 4 days' exposure to bacteriophage in the bowel its undoubted potency *in vitro* is deceptive.

Adams, J. W., and Atwood, R. T. (1944) *War Med.*, **5**, 14.

Barker, P. S. (1943) *Amer. J. digest. Dis.*, **10**, 443.

Boyd, J. S. K., and Portnoy, B. (1944) *Trans. R. Soc. trop. Med. Hyg.*, **37**, 243.

Bulmer, E., and Priest, W. M. (1943) *Lancet*, **2**, 69.

Green, C. A., and Macleod, M. C. (1943) *Brit. med. J.*, **2**, 259.

Jamieson, W. M., Brodie, J., and Stiven, D. (1944) *Brit. med. J.*, **1**, 322.

Roberts, T. L., and Danicls, W. B. (1943) *J. Amer. med. Ass.*, **122**, 651.

Smith, H. G. (1944) *Brit. med. J.*, **1**, 287.

Stanier, Margaret W., and Stapleton, T. (1944) *Lancet*, **1**, 366.

DYSMENORRHOEA

See also B.E.M.P., Vol. IV, p. 353; and Cumulative Supplement, Key No. 367.

Aetiology

Cause

Importance of psychological treatment of nulliparae.—Dysmenorrhoea in nulliparae is almost always due to some cause other than the gross displacement, disease or inflammation of some pelvic organ which is the usual cause of the condition in parous women. Browne points out that the lack of success in the treatment of this type of dysmenorrhoea is due largely to uncertainty as to its aetiology. The various but inadequate theories which have been propounded have produced a variety of forms of treatment. Antispasmodic drugs and hormones are given on the assumption that the pain is due to uterine spasm or, when underdevelopment of the uterus occurs, to a cramp-like, incoordinated uterine action. Likewise, dilatation of the cervix uteri may be indicated if a narrow internal os appears to be causing spasm by obstructing the expulsion of menstrual debris. Another suggestion is that ischaemia of the uterine muscle leads to undue sensitivity of the nerve endings within the muscle. A corrective hyperaemia, however, is not only difficult to produce but, if uncontrolled, may produce excess of pelvic congestion which is itself a possible cause of dysmenorrhoea. Hyperaesthesia, with exaggeration of the ordinary painful sensations, caused by degenerative changes within the ganglia and nerve endings serving the pelvic viscera, is yet another hypothesis which has been put forward. Upon this is based the presacral sympathectomy operation which, when combined with thorough bilateral ovarian denervation, gives satisfactory results in about 85 per cent of cases. It is, however, considered essential to treat each case on its own merits with due regard to the psychological aspect and to restrict operative measures to the severe and incapacitating types of dysmenorrhoea.

The uterus

Painful uterine contractions and primary dysmenorrhoea.—Approximately 35 per cent of women suffer from dysmenorrhoea, either primary or secondary. It is now generally agreed that in primary dysmenorrhoea there is no consistent anatomical lesion although earlier investigators considered that the condition was caused by a lesion such as a retroverted or an infantile uterus, or an ovarian cyst, or by presacral neuritis. Randall and Odell have studied a series of 41 women students with severe dysmenorrhoea; 15 were married and 40 were nulliparous. There was not any consistent demonstrable organic defect or endocrine deficiency and the authors conclude that the pain experienced in primary dysmenorrhoea is due to painful uterine contractions. Ovulation and a nulliparous cervix are 2 essential factors in the production of primary dysmenorrhoea and result in uterine distension which causes contractions of an amplitude sufficient to cause cramp-like pain. The patient should be assured that organically she is entirely normal and the physiological processes associated with menstruation should be explained in simple terms. The pain can generally be relieved by the administration of simple analgesics during the first 2 days of menstruation. Hysterectomy, uterine suspension and presacral sympathectomy are unjustified procedures. Encouraging results can be obtained in most cases by the giving of almost any glandular preparation or placebo and, although in the authors' series of cases 18 out of 20 patients were entirely relieved by the administration of stilboestrol, it is stated that continued suppression of ovulation by oestrogens has not any permanent clinical value and may disturb the pituitary-ovarian balance. After parturition and after the age of 30 years painful menstruation becomes less severe and less frequent and as the menopause is approached the condition becomes anovulatory and painless.

Treatment

General measures

Part played by psychotherapy.—Since a psychic factor appears to play some part in many cases of fundamental dysmenorrhoea, Kroger and Freed suggest that patients who have

painful menstruation may be relieved by psychotherapy under hypnosis. The aim is to raise the threshold of pain so that the sensations conveyed by contractions of the uterus are not registered as pain in the consciousness of the individual. The authors have used hypnosis in 9 cases of functional dysmenorrhoea in which no relief had been obtained from other forms of therapy. All the patients had been examined gynaecologically and there was not any obvious cause for the cyclic menstrual pain. It was considered that latent psychogenic factors were contributory to the intensity of the symptoms and an attempt was made to carry out a short course of psychoanalysis and personality study in 5 cases. By employing the procedure known as hypno-analysis—a rapid form of psychoanalysis under hypnosis—with age regression, each patient was regressed to a pre-adolescent phase or to the age preceding the onset of dysmenorrhoea. Slow reorientation was then induced so that the causation of the emotional conflicts, inhibitions and personality changes could be elucidated. Cure of the dysmenorrhoea was then effected by psychotherapy and re-education under hypnosis. Total amnesia for the entire menses was achieved in some patients. Hypnosis is the method by which treatment can be carried out in such cases and is not the actual means of cure. The disadvantages of hypnosis are few; in the authors' series of patients the results were very satisfactory, since 7 out of 9 were completely relieved and the cure is considered to be permanent. Further trials of the method are advocated.

Browne, O'D. (1944) *Med. Pr.*, **211**, 372.

Kroger, W. S., and Freed, S. C. (1943) *Amer. J. Obstet. Gynec.*, **46**, 817.

Randall, J. H., and Odell, L. D. (1943) *J. Amer. med. Ass.*, **123**, 735.

DYSPAREUNIA

See also B.E.M.P., Vol. IV, p. 361.

Aetiology

Local causes

Psychical and physical considerations in treatment.—Although vaginisms and dyspareunia cause minor or major difficulties in normal marital intercourse, many women fail to receive medical advice for these complaints. Small emphasizes the importance of gaining a patient's confidence and of making a thorough investigation in cases of vaginismus, as many emotional and physiological disorders may thus be prevented. It has been suggested that the condition represents a reflex defence mechanism originating during childhood and caused by trauma. There may also be the fear of degradation and many women complaining of severe vaginismus show other neurotic or psychopathic traits. (1) In mild cases the spasm may be due to a thick rigid hymen; gradual dilatation and the use of lubricants often enables normal coitus to be achieved; (2) in more severe cases in which there is not any organic lesion psychotherapy is often successful; (3) in very severe cases, with spasm of the adductors of the thigh and sometimes episthotonos, caution should be used in attempting investigation since there may be a complete mental breakdown or even suicide. The treatment of dyspareunia is easier than that of vaginismus and there are various anatomical and organic causes. These include urethral abnormalities, congenital vaginal defects, genital disproportion, relaxation of pelvic structures, inflammatory conditions or tumours of the genital organs and rectal lesions. Surgical operations are perhaps the commonest cause of subsequent disability in coitus; perineorrhaphy, episiotomy, cervical amputation, panhysterectomy or other resections may leave painful residual scars or anatomical defects. The interpretation and alleviation of dyspareunia depends upon a complete understanding of the various possible contributory factors and the appropriate treatment in each case.

Treatment

Primary and secondary conditions

Various methods discussed.—Johnstone discusses primary and secondary dyspareunia. Primary dyspareunia, with coitus painful from the first, may be classified as psychopathic or as physiological vaginismus. In psychopathic vaginismus either the idea of intercourse in general is repellent, or the particular partner is repugnant. Treatment by psychotherapy alone is of use in such cases. Physiological vaginismus usually originates from tender areas in the vulva, a resistant hymen, masculine ineptitude, feminine nervousness or physical disproportion. Occasionally, prolapsed ovaries, tubal and ovarian inflammation which has resulted from appendicitis or tuberculosis, or pelvic neoplasms are responsible. Minor cases yield to the application of Dettol ointment. Attempts at coitus should be discontinued for a time, and petroleum jelly with or without 5 per cent cocaine should be employed as a lubricant on its resumption; the husband should be advised against precipitation. Severe cases require anaesthesia for examination and equipment should be at hand for the purpose of stretching the orifice, or for radical excision of a resistant hymen. When healing is complete graduated dilators can be employed in order to overcome vaginismus. First a lubricated dilator of forefinger dimension is introduced by nurse or practitioner and remains in place for 2 hours twice a day while the patient is in bed. Next, introduction of the dilator by the patient herself induces confidence and when tolerance is achieved larger dilators can be used. Administration of oestrogenic preparations sometimes alleviates the frigidity which is associated with fear in hypogonadic women, but because of their effect on menstrual rhythm they must be used with caution. Disproportion may require perineotomy for the purpose of dividing the superficial

fibres of the constricting muscles and levatores ani. Secondary dyspareunia, which begins after previously painless coitus, when superficial suggests infection of Bartholin's glands, urethritis, caruncle, cystitis or vaginitis, the last the result perhaps of trichomonas infection. Kraurosis, leucoplakia, post-operative scar tissue and fistulae are rarer causes. Deep-seated dyspareunia suggests pelvic inflammation as a result of childbirth, or gonococcal infection. Uterine retroversion and ovarian prolapse have also to be considered as causes of secondary dyspareunia.

Johnstone, R. W. (1944) *Practitioner*, **152**, 142.

Smail, C. (1943) *Northw. Med., Seattle*, **42**, 322.

DYSPEPSIA

See also B.E.M.P., Vol. IV, p. 367; and Cumulative Supplement, Key No. 369.

Clinical picture

Functional dyspepsia and its treatment

Investigation and research in the Forces.—Edwards and Copeman report on dyspepsia in troops investigated during one year by a board composed of a physician, a surgeon, a radiologist, a pathologist, and a psychiatrist. Radiographical and gastroscopical evidence, clinical history of hyperchlorhydria and the presence of occult blood or a history of perforation yielded a group of 139 ulcerous cases, 16 being gastric and 121 duodenal. The non-ulcerous group included functional dyspepsia 180 cases, gastritis 23 cases, duodenitis radiologically diagnosed but sceptically regarded 9 cases and 5 others. Fifty-one patients had undergone abdominal operations, 7 operations being for perforation. The remaining 44 operations included 26 for chronic appendicitis without relief, suggesting that a diagnosis of appendicitis is too lightly made. Salient facts regarding pain emerge from analysis. First, of ulcerous patients 72 per cent are relieved by food and 77 per cent by alkalis. Of non-ulcerous patients 43 per cent are relieved by food and 62 per cent by alkalis. Secondly, food affords longer relief to the ulcerous than to the non-ulcerous group. Thirdly, nocturnal pain suggests ulceration and if eating gives relief the explanation is all the more likely. Radiography proved reliable in ulcerous cases. Gastroscopy was valuable in confirmation and in correction, and in revealing gastritis, invaluable. The psychiatrist, investigating 103 patients, found a nervous background in 67, of whom 25 exhibited an anxiety state. The responsibilities of non-commissioned rank and of parenthood cause reluctance in reporting sick for conditions less urgent than ulcer. Discharge from the army was necessary in 119 ulcerous in contrast to 20 non-ulcerous cases.

Edwards, H., and Copeman, W. S. C. (1943) *Brit. med. J.*, **2**, 640.

EAR DISEASES

See also B.E.M.P., Vol. IV, p. 402; and Cumulative Supplement, Key Nos. 374–384.

Foreign bodies and injuries

Violence and explosions

Two-stage effect of blast.—Rüedi discussing the injuries to the ear caused by blast points out that the effect of an explosion is shown in two phases, (1) an initial sudden and momentary increase of air pressure and (2) a more prolonged and gradual diminution of it. The ear is thus subjected to the impact of a sinusoidal wave the amplitude of which depends upon the pressure generated by the explosion and of which both phases show minor oscillations. It may be likened to a wave of water which similarly shows a ridge and a trough with a surface marked by minor ripples. Each phase of the blast wave has a different effect upon the ear. The positive phase, when the explosion takes place at close range, usually results in rupture of the drum or even in its complete detachment from its moorings. The ossicles may be dislocated or broken. Such an injury gives rise to impairment of hearing especially for the lower but also for the highest tones. The wave of blast is transmitted also to the inner ear and may damage the auditory nerve or the organ of Corti. It is doubtful whether the positive or the negative phase is responsible. Injuries to the inner ear as described above carry a much worse prognosis than do those to the middle ear.

Acute otitis media

Causes

Non-purulent effusion.—Clinical observations on acute catarrhal otitis media, complicated by non-purulent fluid in the middle ear, are given in a paper by Hoople and Blaisdell. They call the condition acute secretory otitis media. In 619 out of 748 civilian cases the cause was found to be recent infection of the nose and throat. No evidence of infection was observed in 100 patients; in these allergy, endocrine defects, pregnancy, aero-otitis and trauma were the causative factors. Of 32 army cases almost all occurred after acute upper respiratory infections; 2 were due to blows on the head. In acute secretory otitis media the entire middle ear, not the tympanic cavity only, is involved, and the mastoid cells also are affected. If it is unrelieved the effusion gradually loses its fluid quality. Inflammation, necrosis, ulceration and then infiltration with fibrin ensue and later organized adhesions replace the original matter. As helps to the often difficult diagnosis of fluid, the pneumatic otoscope and the auscultation tube are useful. Cases have been seen in which fluid had been undetected for many weeks. Subacute cases appeared to be the most difficult to clear. Acute cases, when

treatment was begun early, usually cleared up quickly, but when not treated until a later stage, recovery might not take place for months. In patients with acute inflammation the infection was treated first and nothing was done to the ear at that stage. If serum persisted catheterization with gentle inflation was done, and afterwards, if necessary, paracentesis of the tympanum with inflation of the ear. Occasionally gentle suction was used. In cases of non-infective origin search was made for other causative factors and appropriate treatment was instituted. Fifteen cases were not improved after a considerable amount of treatment. Mastoidectomy, which has been recommended in protracted subacute cases, might possibly have cleared these.

Mastoiditis

Analysis of cases.—Analysis by Towson of 526 operations on 466 patients with acute or chronic mastoiditis shows that 65 per cent were performed for acute mastoiditis and 35 per cent for chronic mastoiditis, a ratio confirmed by statistics of 3,225 cases from Bellevue Hospital, New York. Chronic infections of the left side outnumbered those of the right. In the acute conditions lateral incidence was equal and the percentage of males was 52·7 and of females 47·3, percentages approximately reversed in the case of chronic mastoiditis. Bilateral acute mastoiditis affected 18·8 per cent, a figure twice that quoted by other statisticians. Age ranged from infancy to 70 years, the group of from 4 to 12 years being most vulnerable to acute infections and that of from 19 to 30 years to chronic infections. In one-half the number of acute cases the patients underwent operation during the third, fourth and fifth week of known otitis media. Two-thirds of the number of operations occurred during the 6 months January to June. Operations for chronic mastoiditis, less urgent, were spaced throughout the year. Respiratory infections, measles and scarlet fever are the usual origins of acute and, when determined, of chronic mastoiditis. The organisms most responsible are *Streptococcus haemolyticus* especially, streptococci in mixed infections and pneumococci. *Bacillus proteus* was responsible for 8 chronic and for one acute infection. Leucocytosis is usual in acute mastoiditis but high counts indicate severe illness or complications. The count is usually below 12,000 in chronic mastoiditis. Radiology, occasionally misleading, usually gives information confirmed at operation. Exposure of the dura mater on 240 occasions, including often the lateral sinus, proved innocuous. Cholesteatoma, present in 50 per cent of the chronic cases, demands operation. Mortality for all operations was 5·8 per cent, chiefly as a result of meningitis. Combined results traced in 134 patients showed cure in 109 and in 16 persisting discharge. Hearing was reported to be improved by 36 patients, stationary by 59, and as deteriorated by 39. One hundred patients were enjoying better health, previous good health was maintained by 18 and 16 could report no improvement.

Involvement of mastoid bone

Diagnostic significance of presence or absence of pain on pressure.—The clinical evaluation of tenderness of the mastoid process is discussed by Rosenwasser who points out that although persistent tenderness in this region is one of the most significant and constant signs of disease of the mastoid bone, there are nevertheless several factors which may modify the tenderness and absence of tenderness does not preclude involvement of the bone. The modifying factors may be local or general and they should be considered always in deciding whether or not genuine tenderness is present. A patient may be hyposensitive or hypersensitive to pain and therefore the same disease may cause varying clinical pictures in different persons. Young children occasionally react defensively to pressure over the mastoid process and thus give an erroneous impression. In a small number of patients there may be a marked disproportion between the degree of complaint and the physical signs; the diagnosis of neurosis however should be made only on the evidence that the patient is ill emotionally. Moreover a neurosis can exist concurrently with serious organic disease. When mastoiditis does occur in patients treated with sulphanilamide the classical picture is seldom seen, and many typical signs, notably tenderness, are masked. Obscuration or simulation of mastoid tenderness may result from (1) the local effect of irradiation during routine X-ray treatment of the mastoid region, (2) the presence of inflamed lymphatic glands over the mastoid process and (3) the organism responsible for the infection of the mastoid and of the middle ear, especially in patients with diabetes. The time of incidence of mastoid tenderness during suppuration of the middle ear is a significant diagnostic factor. Clinical experience indicates that only too often 2 or more of the above-mentioned conditions may exist concurrently.

Treatment

Dangers of sulphonamide therapy.—Dingley presents some dangers of sulphonamide therapy in ear infections. Acute suppurative otitis media associated with a bulging, pulsating and usually purplish ear drum calls for immediate myringotomy and no dosage with sulphonamides can take the place of this necessary step. Treatment with the appropriate sulphonamide should be reserved for the period after incision, but if after 2 or 3 weeks of otorrhoea the fever or the discharge persists, mastoid drainage is indicated. Sulphonamides mask and distort the clinical picture and may interfere with the acquisition of an immunity to the infection by the patient, with an increase in the possibility of recurrence. The author does not disparage the value of the drugs but emphasizes the importance of a combination of such therapy with surgical procedures. One of three cases reported on proved to be fatal on account of delay in surgical drainage.

Chronic suppuration of the middle ear**Treatment**

Success of sulphonamide compounds.—Lawson believes that the sulphonamide compounds have made possible a notable improvement in the results of the treatment of chronic suppurative otitis media by conservative methods. The efficacy of the various sulphonamide preparations, in relation to the type of bacteria present in the ear, is discussed. The author comes to the conclusion that sulphanilamide (which he uses as a suspension in distilled water, 1 gramme in 30 cubic centimetres) is the preparation of choice because its greater solubility makes possible a greater concentration, and that it is most effective when used in suspension because in that form it adequately maintains bacteriostasis and allows of uninterrupted healing. All the principles of careful cleansing should be strictly observed in order that proper contact with the infected regions may be made. Furthermore it should always be borne in mind that although a fair proportion of chronic disorders of the middle ear will prove to be purely local problems some may be influenced by bodily diseases and deficiencies which need investigation. It would appear that the results of treatment are most striking when there is not any epithelial invasion, although even when this has occurred local therapy with sulphonamide compounds achieves better results than those obtained with any therapeutic agents previously used.

Dingley, A. R. (1944) *Brit. med. J.*, **1**, 747.

Hoople, G. D., and Blaisdell, I. H. (1944) *Proc. R. Soc. Med.*, **37**, 270.

Lawson, L. J. (1943) *Arch. Otolaryng.*, *Chicago*, **38**, 550.

Rosenwasser, H. (1943) *Arch. Otolaryng.*, *Chicago*, **38**, 447.

Rüedi, L. (1943) *Schweiz. med. Wschr.*, **73**, 913.

Towson, C. E. (1943) *Arch. Otolaryng.*, *Chicago*, **38**, 32.

ELECTRICAL INJURY

See also B.E.M.P., Vol. IV, p. 472.

Morbid changes caused by electrocution and lightning stroke**Changes in central nervous system**

Comparison with multiple sclerosis.—Ostow discusses the possible pathogenetic action of electricity in the central nervous system. In certain circumstances the normal strength of the electrical fields in that region may be so increased (potential gradients of the order of one-tenth of a volt being increased to the order of 1 or 2 volts per centimetre) as to cause irreversible tissue damage, either by direct effect on nerve cells or indirectly by the production of ischaemia. The strength of the electrical fields has been found to be greatly increased by the action of strychnine, by tetanus virus and by cold. White matter and the tissues at the various boundaries of the central nervous system are found to be the most susceptible to injury. Although theoretical considerations alone cannot be taken as proof of the pathogenesis of any particular disease they may give pointers towards the line of further investigation. Continued extensions of lesions after the aetiological agent has ceased to work (as for example in carbon monoxide poisoning or in the recurrent exacerbations in cases of epidemic encephalitis) may be due to the creation by a necrotic lesion of a boundary at which electrical fields are particularly effective. Again, because electrical field effects are most apt to occur in myelinated tracts and in the neighbourhood of the various boundaries of the central nervous system, this distribution of lesions strongly suggests the distribution of lesions in multiple sclerosis. Further, according to another observer, experimentally healed electrical lesions in nerves are comparable to the healed plaques of multiple sclerosis in remission.

Ostow, M. (1944) *J. nerv. ment. Dis.*, **99**, 270.

ELECTRODIAGNOSIS

See also B.E.M.P., Vol. IV, p. 484.

Recent methods of testing reactions**Anomalies of muscle testing**

Electrodiagnostic interpretations in nerve lesions are discussed by Bauwens who also gives an account of the technical aspects of muscle testing. For the purpose of obtaining useful information from transcutaneous muscle testing the effect of electrical stimulation on muscles consisting of varying proportions of normal and abnormal fibres must be clearly visualized and it is necessary to appreciate the changes produced by an increase in the number of denervated muscle fibres. The curves which graphically depict successive stages in such changes are shown and are fully explained. The classical method of faradic stimulation is simple but lacks precision. Objections can also be made to the use of galvanic currents since the current tends to fluctuate when passing through the body tissues. The author has devised a special apparatus which can emit single impulses the duration and intensity of which can be controlled. The observations which may be made however require to be carefully weighed and assessed. The author affirms that particular attention should be paid to the effect of injury on the function of the afferent part of the nerve by which the patient is made aware of the existence of the muscles. Misinterpretation due to anomalies of innervation may be

avoided in doubtful cases if the possible alternative nerve is stimulated. Cross-innervation is common in the hand and both the median and ulnar nerves should be tested as a routine. Certain anomalies of muscle testing are discussed. Oedema is always an obstacle to such tests and hyperaemia in muscles produces difficulties similar in kind. Cold slows down contractions and may cause reactions simulating those of denervated muscles; sensory defects may also lead to erroneous conclusions. Deterioration is more easily detected than regeneration and the biochemical processes involved in degeneration are also understood better than those which take place during the regeneration of a nerve axon. A single examination is seldom sufficient for prognostic purposes; usually serial tests are required in order to obtain a true picture of the trend of developments. The complexities of muscle testing should attract the interest of more workers because they present many interesting problems.

Bauwens, P. (1944) *Brit. J. phys. Med. N.S.*, 7, 2.

EMPHYSEMA OF THE LUNGS

See also B.E.M.P., Vol. IV, p. 508.

Chronic obstructive emphysema

Clinical picture

Mechanism of breathing.—Christie states that in emphysema of the lungs the damage to the air sacs and the effect on the volume of the lung are the most serious results to be considered. The term, emphysema, as here used by Christie means chronic vesicular or hypertrophic emphysema of the lungs. The emphysematous lung is deformed in at least 3 ways: (1) the air sacs and the alveolar ducts are dilated; (2) the supporting framework of the air sac may be lost; (3) the amount of air in the lungs is usually increased although the emphysematous lung as a whole is not over-distended. These changes extend throughout the lung substance. There is widespread sclerosis of the pulmonary vessels and obliteration of many capillaries but the total blood flow through the lung is not diminished. Peripheral lymphatic vessels may show cellular infiltration. There is usually kyphosis of all thoracic vertebrae whereas in senile emphysema the curve is usually to be found in the upper dorsal vertebrae. The blood is insufficiently ventilated in emphysema; this insufficiency may be estimated by analysis of the arterial blood since it is this blood which has been ventilated by the lungs. The blood is deficient in oxygen absorption and in carbon dioxide elimination. Inspiration is performed by 'heaving' the chest; expiration instead of being almost a passive act becomes a forced muscular effort owing to the loss of elasticity of the lung as the result of the respiratory obstruction. Gradually parts of the lung become over-distended. The author suggests that it is the wastage of ventilation in the inelastic alveoli and distended bullae which causes the dyspnoea and the defective haemato-respiratory exchange.

Christie, R. V. (1944) *Brit. med. J.*, 1, 105, 143.

ENCEPHALO-MYELITIS

See also B.E.M.P., Vol. IV, p. 553; and Cumulative Supplement, Key No. 400.

Acute disseminated encephalo-myelitis complicating the specific fevers and vaccination

Nervous complications of vaccination, measles, smallpox, chicken-pox and German measles

Encephalo-myelitis in measles.—Reisman and Rosen report on 20 patients with encephalitis complicating measles. They comprise 12 boys and 8 girls, the average age being 5·7 years. The views on aetiology are (1) that the encephalitis is due to the measles virus, (2) that it is an allergic phenomenon and (3) that it is caused by an unknown virus. Congestion and small haemorrhages occur about the blood vessels of the brain and spinal cord, particularly in the white matter. The perivascular cuffing is chiefly by microglial elements. The onset of the symptoms of encephalitis in most of the authors' cases was sudden and occurred from 2 to 6 days after the rash appeared. Stupor, coma and convulsions were common. The cerebrospinal fluid showed a pleocytosis mostly of lymphocytes, with normal protein and normal or increased sugar. Of 18 survivors 2 were examined 4 years later and 8 one year later. Eight patients were quite normal, but 2 showed personality changes with mental deterioration. Treatment was entirely symptomatic. Sedation was used for restlessness and convulsions, but only in a few cases was spinal fluid withdrawn in order to relieve intracranial pressure. In patients with the more severe symptoms hypertonic solution of dextrose was given intravenously. Magnesium sulphate was given intramuscularly. Sulphapyridine when tried had not any apparent effect. Typhoid vaccine was given on alternate days to one patient who had been in a coma for 3 weeks. After 3 doses had been given with a good febrile response the child began to show signs of clearing mentally.

Litvak, Sands and Gibel present a report of 56 cases of encephalitis complicating measles. The incidence cannot be determined correctly but may be taken as about 1 in 1,000 or 1,500 cases of measles. It is believed that there has been an increased incidence within recent years. The cause still remains debatable. The onset may be abrupt with convulsions, or gradual; the average time of onset is from 4 to 6 days after the appearance of the rash. There is no correlation between the severity of the measles and the occurrence of encephalitis. The symptoms are very variable and often vary from day to day. The authors suggest an anatomical classification dependent upon the principal symptoms. (1) The meningeal type, which exhibits

features of meningeal irritation (6 cases). (2) The encephalitic type, which is characterized by convulsions, coma and disturbances of reflexes (35 cases). (3) In the bulbar form (2 cases) cranial nerve disturbances, dysphagia and respiratory and cardiac disturbances are seen. (4) Striatal features are also uncommon (2 cases). (5) The myelitic type involves the spinal cord primarily (1 case). (6) Last comes a heterogeneous group in which there is a combination of the above symptoms (10 cases). The spinal fluid does not present any diagnostic features. The pathological features are characterized by perivascular demyelination and the affected areas are limited to the white matter of the cerebrum, cerebellar peduncles, pons, cerebellum and spinal cord. The process is diffuse. There is severe congestion of the meninges and of the entire nervous system. The authors in discussing prognosis divide their cases into two groups. Thirty-three cases were seen between 1935 and 1941, and of these 4 died; the subsequent history of 17 of the 29 patients who recovered has been investigated and in 11 of these sequelae have been demonstrated. Such features as nervousness, emotional instability, irritability, headaches, enuresis, inability to concentrate, are included in the latter category. The second group comprises 23 patients seen in the 1941 epidemic; 4 died and out of 15 cases of survival investigated 11 showed sequelae. There is no specific therapy.

Post-vaccinal encephalo-myelitis

Value of human immune serum.—Fyfe and Fleming discuss encephalo-myelitis in children after vaccination. In the County of Fife, Scotland, during 1942, free vaccination was accepted by 72,969 persons. Nine cases of encephalo-myelitis occurred. All 9 concerned children between the ages of 3 and 17 years who were vaccinated for the first time. One was suffering from pertussis, so that the possibility of the encephalitis being secondary to that disease could not be excluded. The rest had been in good health before they were vaccinated. The vaccination reaction in each was a single vesicle and was pursuing an apparently normal course. In 6 patients the clinical picture was that of encephalitis; 4 of them died. In 2 patients the clinical features were those of myelitis; both recovered rapidly. In one patient acute lymphocytic meningitis was present; rapid recovery occurred. Immune serum was used in 6 cases. Two of the patients received horse serum and 4 had serum from parents who had just been revaccinated. The parental serum appeared to be of great value; in one child it was probably given too late and this patient died. The authors suggest that whenever primary vaccination of children other than infants is necessary the parents should be vaccinated at the same time so that suitable immune serum is available. The value of horse serum is debatable.

Spontaneous encephalo-myelitis

Conditions of transmission

Analysis of a laboratory infection.—Lennette and Koprowski report a series of cases in which the ability of the Venezuelan equine encephalitis virus to infect man was clearly shown. In these 8 human cases of laboratory infection with the Venezuelan virus, the disease varied from a mild illness to a severe infection with involvement of the cerebral nervous system. All 8 reacted immunologically to the Venezuelan virus and in 6 cases the virus was recovered. No fatalities occurred although this virus is the most virulent for laboratory animals of the three equine encephalo-myelitis viruses. Epidemiologically it has been shown that the western equine virus is arthropod-borne and potential mosquito vectors have been reported for both the eastern and the Venezuelan equine viruses. The evidence in favour of arthropod transmission excludes almost entirely the possibility of the virus being borne by contaminated water or food or by contact. The authors, however, recovered the specific virus from the nasopharynx of 2 of their cases, so that transmission by contact is possible. The importance of the part such transmission plays in the epidemiology of human infections provoked by the equine encephalo-myelitis viruses has yet to be investigated.

Fyfe, G. M., and Fleming, J. B. (1943) *Brit. med. J.*, **2**, 671.

Lennette, E. H., and Koprowski, Hilary (1943) *J. Amer. med. Ass.*, **123**, 1088.

Litvak, A. M., Sands, I. J., and Gibel, H. (1943) *Amer. J. Dis. Child.*, **65**, 265.

Reisman, H. A., and Rosen, A. S. (1943) *Amer. J. Dis. Child.*, **66**, 597.

ENDOMETRIOSIS AND ADENOMYOMA

See also B.E.M.P., Vol. IV, p. 561; and Cumulative Supplement, Key No. 401.

Clinical aspects

Treatment

Testosterone propionate.—At a meeting of the Philadelphia Obstetrical Society, Hirst gave reasons for trying testosterone propionate therapy in advanced cases of endometriosis when radical operation is contra-indicated, impracticable or refused and described the favourable response obtained in 2 cases of this kind. The progesterone-like effect of androgens in suppressing or neutralizing oestrogens is well recognized and it is reasonable to hope that they might inhibit the proliferation of endometrial tissue. Of the 2 patients reported on by Hirst one was a married woman aged 33 years complaining of sterility. A diagnosis of adherent, acutely retroflexed uterus was made and operation undertaken; a chocolate cyst of the right ovary was discovered and removed. Recurrence took place 2 years later in the left ovary. The cyst became steadily larger during the ensuing 9 months and as further operation was

refused, treatment by intramuscular injections of testosterone propionate, 125 milligrams a month, was begun. The cyst continued to grow and after 3 months the dosage of testosterone propionate was increased to 25 milligrams every third day. A month later the cyst was distinctly smaller. Treatment is being continued. The second patient, an unmarried woman aged 23 years was admitted to hospital with an 'acute abdomen' and operation disclosed a ruptured right ovarian endometriomatous cyst. Five years later there developed acute intestinal obstruction, found at operation to be due to adhesion of the ileum to an endometriomatous cyst of the left ovary. The cyst was emptied and the obstruction relieved, permission to resect the ovary having been refused. Two years later a recurrent mass was found in the left lower abdomen and intramuscular injections of testosterone propionate were begun. Doses of from 100 to 150 milligrams a week were continued for 6 months resulting in relief of pain and considerable retrogression of the mass.

Hirst, J. C. (1943) *Amer. J. Obstet. Gynec.*, **48**, 97.

ENDOMETRITIS, CERVICITIS AND METRITIS

See also B.E.M.P., Vol. IV, p. 574.

Bacteriology of normal vagina

Döderlein's bacillus

Variations in glycogen.—Rakoff, Feo and Goldstein preface a biological investigation of the vagina by recapitulating the structure of its mucosa. On the connective tissue which constitutes the tunica propria lies the stratum basale, divided into a dark zone and a wider light zone. Next comes the intra-epithelial cornification zone of Dierk which underlies the superficial zona functionalis. The influence of oestrogens and progesterone on these strata and their glycogen content, as assessed by smears and biopsy, with investigation of the vaginal flora and hydrogen ion concentration, form the objectives of this research. Oestrogen is active during the reproductive period and especially during advanced pregnancy and concurrently with oestrogenic activity the mucosa proliferates. This proliferation, as a cyclic change, is most pronounced at the mid-cycle and in the dark zone. Nevertheless the simultaneously increased glycogen storage occurs in the superficial layers. Conversely, during childhood and after the menopause the vaginal epithelium is attenuated and glycogen is absent. Progesterone is probably adjuvant, according to clinical evidence, although experimentally its effect seems partially inhibitory to oestrogens. The administration of androgens is wholly inhibitory to cell proliferation and to glycogen storage. Biopsy illustrates well the distribution of glycogen in the mucosa, but its increase in the superficial epithelium from the beginning of the cycle until its sudden decrease immediately before menstruation shows best in iodine-stained smears. Glycogen is the reputed source of vaginal acidity and its conversion into lactic acid has been attributed to enzymes, to Döderlein's lactobacillus, to the two combined and to the combined action of enzymes with other bacteria. Sterile at birth, the vagina, still influenced by maternal oestrogens, within two days is inhabited exclusively by Döderlein's bacillus. Maternal influence fades within 10 days and allows the influx of staphylococci, streptococci and coliform and diphtheroid bacilli, which persist until puberty. Döderlein's lactobacillus then reappears for the span of fertile life, during which three grades are recognizable. In grade (1) Döderlein's bacillus alone is present; it is accompanied in grade (2) by other organisms. In grade (3) other organisms have ousted Döderlein's bacillus. The ideal grade (1) was correlated with an average vaginal hydrogen ion concentration of 4.56 and the less satisfactory grade (2) with an average of 5.09 per cent. In grade (3) which approaches a pathological state, 5.54 per cent was the average. The estimations, made with a glass electrode connected with a Beckman pH-recorder, showed a gradual diminution of acidity from the anterior fornix to the vulva and a cyclic increase of acidity towards the menstrual mid-cycle. Oestrogens encourage glycogen deposit on which depends the acidity which is correlated with a healthy bacterial content.

Rakoff, A. E., Feo, L. G., and Goldstein, L. (1944) *Amer. J. Obstet. Gynec.*, **47**, 467.

ENDOSCOPY OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS

See also B.E.M.P., Vol. V, p. 1; and Cumulative Supplement, Key Nos. 407-411.

Direct tracheo-bronchoscopy

Uses and indications

In post-operative lung complications.—In a Discussion on bronchoscopy in the prevention and treatment of traumatic and post-operative pulmonary lesions, Canfield said that he considered bronchoscopy to be useful in clearing up obscure chest conditions which might be due to foreign bodies or to growths in the bronchi, in preventing and treating lung complications and atelectasis, in pulmonary medication and in blast injuries. Nosworthy stressed prophylactic measures and simple postural methods of treatment in the prevention and cure of traumatic and post-operative lung complications. He considered endotracheal intubation to be easier, and a soft wide-bored tube less unpleasant for the patient than a bronchoscope. Since 'blind' aspiration is so often successful it should be tried first. Sellors considered the cough mechanism to be most important; anything which interfered with this should be

guarded against. Pain and shock frequently affected the cough reflex. In all chest operations a bronchoscope should be at hand. Blind intubation was often valuable and could be used by less skilled operators. Negus discussed the relative importance of the obstructive matter (mucous, liquid or clotted blood or a foreign body) and the danger of continuous infection, increased by inhibition of ciliary action, so long as the obstruction persisted. Brock queried how often aspiration of the bronchial tree was really needed, and said that ordinary simple methods of prevention of retention of secretions were often neglected. Much harm could be done by excessive suction. Mushin said that the Nuffield Department of Anaesthetics at Oxford kept careful record of all patients during the post-operative period. Most patients with atelectasis recovered under postural treatment, with breathing exercises and free movement, but feeble patients could not be so treated and needed tracheal suction. Gordon described a case of severe head injury in which the left bronchus repeatedly filled up with white frothy fluid although as often removed by suction. At necropsy neither trauma nor pneumonia was found in trachea, bronchi or lungs.

Canfield, N., Nosworthy, M. D., Sellors, T. H., Negus, V. E., Brock, R. C., Mushin, W. W., and Gordon, R. A. (1944) *Proc. R. Soc. Med.*, **37**, 301.

ENOPHTHALMOS AND EXOPHTHALMOS

See also B.E.M.P., Vol. V, p. 42.

Enophthalmos

Causes

Importance of orbital fracture.—Pfeiffer discusses the nature of enophthalmos which develops after injury. In earlier times it was difficult to conceive of a blow to the eye which could produce a fracture of the orbit with little effect on the eye-ball itself. The author has noted a fracture of the orbit in every case of traumatic enophthalmos over a period of 10 years. Out of 53 cases 29 showed external deformity, but in the remainder the fracture was internal or deep in the orbit, unassociated with deformity of the orbital margin; there was displacement of the eye of variable degree and usually posteriorly. Haemorrhage, oedema or air in the orbit usually obscured the displacement until 2 or 3 weeks had passed. Patients who exhibit signs of a 'black eye' should have an X-ray examination for signs of internal fracture of the orbit. The floor, which is of very thin bone, was broken in every case, the posterior portion being affected in less severe and the entire floor in cases of severe displacement. The effect of the fracture is to increase the capacity of the orbit and to allow tissue prolapse. Treatment may not be needed in mild degrees of enophthalmos but when the latter is severe operation for the purpose of raising the orbital floor may be indicated. If diplopia is present in mild degrees of enophthalmos the simpler means of relief may be operation on the extra-ocular muscles.

Pfeiffer, R. L. (1943) *Arch. Ophthalm.*, N.Y., **30**, 718.

EPILEPSY

See also B.E.M.P., Vol. V, p. 96; and Cumulative Supplement, Key Nos. 424–432.

Aetiology

Lesions of the brain

Focal symptomatic epilepsy caused by antidiphtheritic serum.—Moore describes the case of a man of 32 years of age who complained of periodical attacks of paroxysmal pain involving the entire abdomen. The attacks lasted for two hours or more and were associated with flatulence but not with nausea or vomiting; they were first experienced when the patient was 9 years of age and continued at irregular intervals. They occurred more frequently in times of nervous stress and had recently taken place about once a week. No cause had been found for the attacks although the patient had been studied in many hospitals. Physical and laboratory examinations were negative. In view of the periodicity of the attacks and failure of the patient to respond to any form of medical treatment it was decided to have an electroencephalogram made. This showed low voltage abnormal waves, particularly in both frontal regions, increased with hyperventilation. The cerebral dysrhythmia was minimal in degree and such as might be shown by a small percentage of non-epileptics. Medication with phenytoin sodium and bromide was however successful; the patient had remained free from attacks for 15 months since it was started except when it was intermitted. Encephalograms now show restoration of alpha activity. The case is regarded by the author as one of focal symptomatic epilepsy. The cause is believed to have been an injection of anti-diphtheria serum, which was given to the patient shortly before the attacks started. This may have produced cerebral angioneurotic oedema and permanent changes in the brain tissue. Evidence now exists that frontal lobe lesions can produce gastro-intestinal disturbances.

Diagnosis

Differential diagnosis

Electroencephalographic classification.—Gibbs, Gibbs and Lennox have classified according to frequency and wave-form routine encephalograms of 1,260 epileptics and 1,000 adult controls. Eighteen groups can be recognized of which 9 are regarded as normal, 2 as slightly

abnormal and 7 as very abnormal. The distribution of types among the control subjects forms a simple curve with the mode, including 19.9 per cent of individuals, at 10 per second. Among a random sample of 730 epileptics the distribution is bimodal, with modes to the fast and slow sides of 10 per second. During a seizure characteristic patterns are observed corresponding to the 3 types of seizure, (1) *petit mal*, (2) psychomotor and (3) *grand mal*. Waves of the appropriate type appearing in the encephalogram are a valuable diagnostic point. It must be recognized however that in only 48 per cent of epileptics can a routine encephalogram be expected to show these appearances.

Gibbs, F. A., Gibbs, Erna L., and Lennox, W. G. (1943) *Arch. Neurol. Psychiat.*, Chicago, 50, 111.

Moore, M. T. (1944) *J. Amer. med. Ass.*, 124, 561.

EPIPHYSES, DISEASES AND INJURIES

See also B.E.M.P., Vol. V, p. 127.

Osteochondritis

Pseudo-coxalgia

The aetiological problem.—Gill traverses the evidence of thyroid deficiency offered in 1936 by Cavanaugh, Shelton and Sutherland in 5 cases of osteochondritis of the capital femoral epiphysis. The cycle of Perthes's disease has a degenerative phase which lasts for about eighteen months and a regenerative phase which extends over 2 or 3 years. Treatment by prevention of weight bearing shortens the cycle but the evidence presented by Cavanaugh and his colleagues that thyroid administration hastens the beginning of the regenerative phase is insufficient. Schaefer and Purcell's statement regarding juvenile osteochondritis that 'Basic treatment is adequate thyroid therapy. Orthopaedic procedures are secondary or adjunctive', is untenable respecting Perthes's disease. Cretinism apart, the diagnosis of hypothyroidism depends upon skeletal defects, delayed ossification and dentition combined with mental and physical inactivity and supported by biochemical findings in basal metabolism, in serum cholesterol and phosphatase and in creatine excretion. Further, in hypothyroidism in children the pronounced fall in blood cholesterol which lasts up to 70 days after administration of thyroxine is considered by Wilkins to be most significant. In 20 children with Perthes's disease here investigated, neither history nor physical examination nor laboratory tests suggested hypothyroidism. In 4 children who alone displayed disparity in bone development and chronological age the basal metabolic rate and the blood cholesterol were inconsistent with thyroid deficiency. Low basal metabolic rates of -24 and -28 (found in 2 children only) were nullified by normality in blood cholesterol, bone age and clinical evidence. A dose of 3 milligrams of thyroxine was administered hypodermically to 3 patients and to 2 controls with normal serum cholesterol. The ensuing fall in serum cholesterol was of minor degree and it returned to the previous level within 22 days. The cases investigated disprove thyroid deficiency as the sole cause of osteochondritis juveniles but do not dispute a possible multiplicity of causes.

Gill, A. B. (1943) *J. Bone Jt Surg.*, 25, 892.

ERUPTIONS, ANOMALOUS AND ATYPICAL

See also B.E.M.P., Vol. V, p. 146.

Alterations in the vessels

Familial haemorrhagic telangiectasia

Aetiology and treatment.—Figs and Watkins report the occurrence of hereditary haemorrhagic telangiectasia in 12 males and in 8 females over a period of 20 years at the Mayo Clinic. The appellation connotes localized angiomas affecting the nasal and the oral mucosa, the face, neck and thorax and more rarely any epithelial or mucous surface. Essential haematuria has been attributed to this cause. Heredity, not necessarily in unbroken line, is a prominent feature. The blood coagulates normally, and responsibility for haemorrhage, notably epistaxis, rests on the extreme tenuity of the capillary walls. Epistaxis, sometimes fatal, may assume the form of oozing which lasts for several days or of profuse haemorrhages, spontaneous or initiated by sneezing and strain. Secondary anaemia results, this increasing the haemorrhagic tendency, and transfusion, although not curative, may be required. For immediate control of epistaxis, the patient should carry Hurst and Plummer's modification of the Cooper Rose inflation plug consisting of a rubber finger-stall bound over the end of a small catheter. This appliance is lubricated, inserted deeply into the nostril and inflated by mouth or by rubber bulb. For permanent treatment electro-coagulation in which cocaine or, if necessary, general anaesthesia is used is to be preferred to the actual cautery and to trichloroacetic or chromic acid. Radium produces an undesirable atrophy of the mucosa and snake venom is here ineffective. Unfortunately the obliteration of one haemorrhagic area is nullified by the prompt appearance of fresh angiomas in adjacent mucosa but therapeutic measures sometimes result in restoration to active life.

Figs, F. A., and Watkins, C. H. (1943) *Proc. Mayo Clin.*, 18, 418.

ERYTHEMA

See also B.E.M.P., Vol. V, p. 159; and Cumulative Supplement, Key No. 442.

Clinical Picture*Erythema due to internal causes*

Erythema nodosum regarded as a sarcoidosis.—Radiographical studies of the chest, including tomography, made by Kerley in 37 adult patients with erythema nodosum lead him to conclude that the disease is a sarcoidosis. X-ray evidence of recent pathological changes was found in 28 patients; 17 had enlarged bronchial glands with associated areas of nodular infiltration in the lungs, 8 had enlarged glands without pulmonary changes and 3 had pulmonary changes without glandular enlargement. The enlarged glands were in most cases bilateral, the pulmonary changes unilateral in about half the number of cases. One patient's chest had been examined by X-rays shortly before erythema nodosum developed and no abnormality had then been found. In the cases with combined glandular and pulmonary lesions both were usually seen at the first examination, but in 4 cases the pulmonary changes appeared only after 4 or 5 months when the glands were becoming smaller. Against the allergic theory of the aetiology of erythema nodosum are the following points: the disease in Europe is almost confined to the Nordic races; the incidence is seasonal, reaching a peak in April, May and June; it occurs in small epidemics in schools and other institutions; it is limited to certain age groups. Against a tuberculous aetiology is the absence of evidence of clinical tuberculosis in any of the author's cases; the radiographical appearances are not those of tuberculosis but are identical in every way with those described in sarcoidosis. None of the patients showed phalangeal changes or splenomegaly; these however are not invariably found in sarcoidosis.

Kerley, P. (1943) *Brit. J. Radiol.*, **16**, 199.

ERYTHRAEMIA

See also B.E.M.P., Vol. V, p. 176; and Cumulative Supplement, Key No. 443.

Clinical picture*Complications*

Haemorrhage and leukaemia.—Tinney, Hall and Giffin analyse 163 cases of erythraemia especially with regard to the occurrence of post-operative haemorrhage or leukaemoid changes in the blood picture which may resemble myelocytic leukaemia. In the authors' cases haemorrhage occurred in 52 (32 per cent), 28 of the patients being males and 24 females; in 17 cases haemorrhage followed operation; purpura occurred in 13, epistaxis was noted in 12 and gingivitis in seven instances; haematuria, haemoptysis, menorrhagia and subconjunctival haemorrhages occurred in other cases. Splenomegaly occurred in 15 patients with a leukaemic reaction. The peripheral blood showed a leukaemoid reaction in 28 patients (17 per cent). The authors record a case of general enlargement of the lymphatic glands and considerable splenomegaly. Patients with the disease for the longest time had the most prominent splenic enlargement and leukaemic reaction.

Occurrence of koilonychia and treatment by X-rays.—The association of koilonychia, microcytic anaemia and glossitis has been recognized since 1913; a new case of koilonychia and polycythaemia vera is reported by Glazebrook. In koilonychia the nails are spoon-shaped with the distal edge everted, and they may be striated and brittle. In the author's case a woman, 56 years of age, had suffered from duodenal ulcer and when first seen had an enlarged spleen; the erythrocyte count was 7,000,000 and the haemoglobin was 115 per cent. A year later the finger-nails became brittle and typically misshapen, and glossitis developed. The erythrocyte count rose to 8,610,000 but after X-ray irradiation given in a course of 9 treatments with 100 r at each sitting, the erythrocytes fell to 6,450,000 and by the end of 10 months to below 6,000,000. Healthy nails then appeared to be growing and the spleen was much smaller. Five months later symptoms recurred; the erythrocyte count was then 8,500,000 and the haemoglobin 140 per cent. Improvement was however again noted after X-ray irradiation and the serum-iron increased from 0.05 to 0.32 milligram per cent. The syndrome of koilonychia, hypochromic (microcytic) anaemia, achlorhydria and glossitis appears to occur particularly in middle-aged women. The nail dystrophy is of diagnostic importance, but cannot be due to anaemia. Koilonychia and minor nail dystrophies are probably due to serum-iron deficiency, which some authors regard as a causal factor of anaemia.

Glazebrook, A. J. (1944) *Edinb. med. J.*, **51**, 65.

Tinney, W. S., Hall, B. E., and Giffin, H. Z. (1943) *Proc. Mayo Clin.*, **18**, 227.

EYE EXAMINATION

See also B.E.M.P., Vol. V, p. 216.

Instruments and technique of using them*Orthoptic instruments*

Major amblyoscope, stereorthopter and rotoscope.—The use of orthoptic instruments is

discussed by Stark with especial reference to the major amblyoscope, the stereorthopter and the rotscope. Major amblyoscopes are constructed on the principle of the Worth amblyoscope and have a wide lateral range in order to permit compensation for convergence or divergence. Accurately calibrated scales and an illuminating device are additional improvements. The treatment of abnormal retinal correspondence in many patients with strabismus is important and major amblyoscopes are of use in this connexion both for diagnosis and for correction. The study of corneal reflexes is also of great value when fusion amplitude is being developed in patients with normal retinal correspondence: the loss of fusion may be detected by the observer before the patient is conscious of diplopia. The stereorthopter however does not provide any means for conducting exercises with varying accommodation and the major amblyoscope cannot be used for the measurements and fusion amplitudes in the vertical fields. It is pointed out that in the orthoptic training of young children, the patient must cooperate with interest and with ability since no instrument can correct muscular imbalance if the child fails to concentrate his attention on the target. Such targets should depict objects of interest to children and should be brightly coloured. The stereorthopter is a cumbersome apparatus and is less precisely calibrated than is the major amblyoscope. The use of the stereorthopter provides exercises for the maintenance of binocular vision in cases of slight noncomitant deviation and for the development of fusion amplitudes, especially of convergence. With this instrument, also, it is possible to diagnose abnormal retinal correspondence. The rotscope is made in two models, the standard and the royal types, the latter being more elaborate and more expensive. The use of the rotscope is limited to the treatment of lateral deviations with normal retinal correspondence. The status of retinal correspondence cannot be estimated or corrected by this instrument and must be determined by other means before binocular treatments are given. The rotating targets of the rotscope are especially useful for the correction of vertical imbalance and for the provision of rotational exercises in lateral deviation for the purpose of increasing the facility of adjustment.

Routine examination

Contact lenses instead of spectacles

Williamson-Noble points out that although contact lenses are considered to be a modern discovery they were first described by Thomas Young in 1801. Messrs. Zeiss in 1911 introduced ground glass as opposed to blown glass. These lenses suffered from two defects. First, they were afocal and consequently either pressed against the cornea in myopic eyes or in hypermetropic eyes left a space of variable depth. Secondly the scleral portion was ground to a spherical curve and consisted of a relatively narrow rim, whereas as large an area as possible of the bulbar conjunctiva must be used if comfort is to be achieved. The ideal procedure would be to take a mould of the anterior surface of the eye-ball and to construct a contact lens the internal contours of which conformed to the mould. Dallos perfected a method by using a hydrophilic colloid, negocoll. A thin glass shell of approximate fit was filled with liquid negocoll and applied to the cocaineized eye-ball. The material solidifies in 3 minutes and a mould is thus obtained, serving as a model from which a contact lens can be made. Even this method does not provide a perfect fit since a certain amount of deformation of the eye-ball is unavoidable. The modern practice is to utilize the large numbers of individually fitted contact 'shells' available, grouped according to size, shape, depth and curvatures. An approximate fit is tried; layers of glass are ground away until an accurate pattern is obtained. The only way of checking whether or not all opposite half-meridians or sectors are in balance is to draw a horizontal line across the lens and see if this line stays in correct position as the eye moves. The process of fitting is an elaborate one and as many as 20 or more attendances may be required. The advantages of contact lenses over ordinary spectacles are that they (1) move with the eye, (2) are closer to the eyeball, (3) afford protection to the eyes in industry and are almost impossible to break and (4) are prevented from fogging by movements of the lids; furthermore, they are invisible and they cannot be knocked off. When the surface of the cornea is not spherical contact lenses are indicated since ordinary spectacle lenses are often of little value in improving vision. At first the contact lens may prove a source of irritation and the patient may require to go through a routine training in order to learn how to use them correctly. The reaction of the corneal epithelium to prolonged wear of a contact lens produces dimness of vision in daylight and a halo of coloured rings around lights at night—'Sattler's veil'. The veil disappears in from 10 to 30 minutes after removal of the contact lens. The best procedure in order to overcome the defect is from the first to remove the lenses 1 hour after the veil appears; perseverance in the practice will extend the daily wear for from 12 to 16 hours. The value of plastic materials for contact lenses is undergoing investigation at present. Williamson-Noble envisages a future when contact lenses will perhaps completely replace ordinary spectacles.

Stark, Elizabeth K. (1943) *Amer. J. Ophthal.*, **26**, 1308.

Williamson-Noble, F. A. (1944) *Practitioner*, **152**, 82.

EYE, HEREDITARY DISEASES

See also B.E.M.P., Vol. V, p. 229.

Inheritance of errors of refraction*Visual ability*

Need for orthoptic treatment.—Kuhn states that in the war production effort the increasing demand for munitions of all kinds made necessary the evaluation of the part played by the eyes in production. A direct correlation was found between accuracy and visual perfection and between lost time, accidents and visual defects. Data for an employee's visual ability included visual acuity, stereopsis and colour sense with special tests for intricate work. In 1943 it was found that the percentage rate of defects in civilian applicants was double the 1940 rate. According to Kuhn the ophthalmologist must find new and speedy methods of eye testing so as to make available, for work requiring fair vision, the large class of persons with visual defects who must now work in the new production plants. In an average group of 100 examined in one day there were 35 with defects. Of these 28 were brought to normal visual acuity by the wearing of proper glasses; 7 were rejected because of eye disease. The 28 men would otherwise have been lost to this industry which urgently required top visually-qualified workers. Kuhn also urges that refractive errors be corrected for the particular job the worker is doing. Orthoptic training should be given in suitable cases. She stresses the importance of diagnosing and treating workers as speedily as possible and of keeping a sharp look-out for epidemic keratoconjunctivitis. Ophthalmologists should encourage parents to have their child's squint treated so that the choice of a career later on will not be hampered by defective sight.

Kuhn, Hedwig S. (1943) *J. Amer. med. Ass.*, **123**, 1085.

EYELIDS, INJURIES AND DISEASES

See also B.E.M.P., Vol. V, p. 239.

New formations*Epithelioma*

Four groups differentiated.—Hollander and Krugh review their experience with cancer of the eyelid, which occurs in 9·1 per cent of all forms of skin carcinoma. The morphological features varied widely in their series and the types were well illustrated. The differential diagnosis is discussed. Microscopically four groups were differentiated: (1) basal-celled or hair matrix type, (2) squamous-celled or epidermoid type, (3) mixed cell type and (4) the melanoma group. In prognosis it is important to know the type since if a basal-celled type is completely removed the chance of recurrence is nil, whereas such an optimistic outlook does not hold for the other three groups. Of the authors' 125 patients, 47 were in the seventh decade of life and 82 in the age group from 55 to 74. Whenever possible cancer of the eyelid should be excised. Excision is not possible if the tumour has invaded the surrounding structures to any extent. Furthermore, repair must be of such nature that the eye-ball is not exposed unduly. When the entire thickness of the eyelid is involved, repair becomes difficult. Careful repair of the palpebral conjunctiva is imperative and ectropion must be avoided. Repair of lesions of the inner and outer canthus regions is relatively less difficult since pedicle grafts from the adjoining skin may be used. Radio-knife excision was employed in 12 instances; in 9 cases the results were good but in the others unsatisfactory. Electrodesiccation by means of unipolar diathermy was employed when the growth was infiltrative in character; of 13 cases so treated 7 yielded good and 6 bad results. Inoperable cases and those which presented a poor surgical risk were treated with X-ray irradiation. Combined methods were also employed. Analysis showed a satisfactory result from all forms of therapy in 97 out of the total 125 patients.

Operations*Review of operative measures*

Principles of lid construction.—Sugar gives a brief account of the various methods which have been developed for the reconstruction of eyelid defects. Landolt's lid splitting technique was used for the obtaining of skin to cover defects in the lower lid in cases in which part of the conjunctiva remained. Köllner mobilized a rectangular tarso-conjunctival flap from the upper lid, and sutured it in place in the lower lid defect; the skin defect was grafted. Kuhnt's automarginoplastic operation is useful in cases of tumour of the lid margin; the skin round the tumour is incised in the form of an arch and two incisions are made in the conjunctival surface perpendicular to the lid margin and a third is made parallel to it beyond the growth. The flap is used to fill the gap. For partial defects of the upper lids, Ferris Smith split both lids, and rotated a tarso-conjunctival flap from the lower to the upper lid; the skin defect was made good by a skin flap. Dupuy-Dutemps's operation for lower lid defects consisted in splitting the lids, uniting the layers, and later skin-grafting the defect. Finally, the palpebral opening is re-established by a through and through incision along the ciliary border. In Hughes's operation for lower lid defects the skin of the cheek is utilized and a strip of hair-bearing skin from the opposite brow is used to form the lashes. Imre and Blascovics used sliding flaps obtained from the cheeks by means of curved incisions; Burow's cutaneous triangles are removed at the ends of the incisions as necessary. The author stresses that the important principles of lid construction are (1) lid splitting; (2) the use of Imre sliding flaps with Burow's triangles; (3) the Wheeler hair-bearing graft transplant to form lashes; (4) the Wheeler prin-

ciple of 'halving' whereby the skin and tarso-conjunctival layers are united at different levels in order to minimize scar contraction.

Hollander, L., and Krugh, F. J. (1944) *Amer. J. Ophthalm.*, **27**, 244.

Sugar, H. S. (1944) *Amer. J. Ophthalm.*, **27**, 109.

FALLOPIAN TUBES DISEASES

See also B.E.M.P., Vol. V, p. 250.

Tubal pregnancy

Clinical types

Intra-uterine and extra-uterine pregnancy occurring at the same time.—King reports an obstetric case with the unusual combination of an extra-uterine with an intra-uterine pregnancy. He says that these cases may be of two types: (1) combined or simultaneous and (2) compound. (1) The combined type (as in the author's case) is probably the same as a multiple pregnancy except that one or more implantations are extra-uterine. The extra-uterine pregnancy may be symptomless until the eighth week, or it may proceed to term and even produce a viable foetus. The intra-uterine part of this pregnancy may abort or miscarry or may go to term with a normal living child. (2) In the compound type the extra-uterine pregnancy may have been present for a long time and is usually symptomless and dormant. A normal intra-uterine pregnancy may quite well occur in such a case, but the author states that there is no clear evidence that an extra-uterine pregnancy ever superimposes itself upon an existent intra-uterine pregnancy. The quiescent (mummified or calcified) extra-uterine product of conception may only be discovered on examination for or at operation for a suspected abdominal neoplasm. Therefore it is the combined type, with the danger of rupture of a tubal pregnancy, which presents a clinical emergency. Suitable treatment at the right time may save the life of the mother and of the intra-uterine foetus.

King, S. J. (1943) *New Engl. J. Med.*, **229**, 965.

FIBROSITIS

See also B.E.M.P., Vol. V, p. 279; and Cumulative Supplement, Key No. 489.

Clinical picture

General symptomatology

The myalgic spot.—The myalgic spot is a hyperaesthetic area in a muscle or in its sheath which when stimulated causes pain, local or referred. Copeman contends that these spots are precursors of the fibrositic nodule and should be treated. Such spots are multiple and are situated in the lumbar and gluteal muscles or sometimes elsewhere. Kellgren has described the distribution of their radiating pain. In an epidemic of influenza conforming to the type described by Horder and Gow and recently studied, lumbar pain was a prominent symptom. Of 40 patients not one reported that he had had rheumatism before. Severe pain simulating lumbago radiated from focal points. In half the number of patients examined, although subjective pain disappeared within 3 days, pressure on the myalgic spots elicited sharp pain throughout the area previously affected. Time caused progressive diminution in the number of painful spots and 2 months later not one was found in 50 per cent of the patients. Subsequent infections of other origin may again induce pain in the spots and 3 cases are detailed in illustration. In case (1) mumps occurring 3 weeks later caused 2 days of lumbar pain. In case (2) sand-fly fever, artificially induced by permission a fortnight later, gave rise to a recrudescence of similar pain and in case (3) a common cold caused recrudescence. Moreover in other infective diseases, notably glandular, undulant and scarlet fevers, measles and rubella, these myalgic spots may be originated. Probably chill, damp, trauma and focal sepsis, formerly held to be causative, act by rekindling the latent spots of previous disease causing a local oedema which the skilled masseur is able to disperse.

Panniculitis

Weber-Christian disease.—Two instances of spontaneous subcutaneous fat necrosis (Weber-Christian disease) are recorded by Keiser. (1) In 1934 a woman aged 40 years had a thrombosis of the right leg after pneumonia, which was followed by the development of a red, hard swelling in the right thigh. The hardness persisted. Shortly before she was first seen by the authors she had an attack of influenza; the indurated area again became painful and red. On examination she had a flat, hard swelling attached to the skin. It was excised and found to consist of lobules of fat separated from one another by coarse strands of fibrous tissue and exhibiting necrotic and cystic areas towards their centres. Fatty debris and large phagocytic cells containing fat droplets were present in the necrotic areas, which also showed inflammatory infiltration. (2) A woman aged sixty years had noticed for the previous ten years a hard, painful area in the right buttock and for four years several similar nodules in the left buttock. Shortly before she was first seen other patches had appeared in both arms. An excised nodule showed histological characters similar to those observed in the first case, but without inflammatory infiltration. The aetiology of the condition, which affects women almost exclusively, is unknown.

Bursitis

Sclerosis and drainage.—The conservative treatment of chronic bursitis by the injection of

sclerotic agents in conjunction with the use of drainage is described by Cottrell, who has devised a new technique which reduces the time required for the purpose of achieving a cure. Various types of bursitis were encountered among shipyard workmen including 30 cases of olecranon bursitis, 18 cases of prepatellar bursitis, and 2 cases of semimembranosus bursitis (Baker's cyst). Secondary complications such as acute haemorrhage in the sac, infection and chronic effusion were seen and appropriate preliminary treatment was given. Chronic bursitis with effusion was treated by the obliteration method with continuous drainage of the sac by a special type of rubber drain. In some cases sterile aspiration and the application of a compressive dressing was sufficient. When this method failed obliteration by chemical agents was effected under local anaesthesia. The sclerosing solutions used included sodium morrhuate (5 and 10 per cent), tincture of iodine (6.5 per cent), proliferol solution (synnasol) and sodium psylliate (5 per cent). The last-named proved to be satisfactory for routine use. From 2 to 4 cubic centimetres of the solution was injected into the sac after preliminary drainage of the sac contents. The solution was drained off after an interval of from 5 to 10 minutes. The rubber drain was left in situ for from 48 to 96 hours and a pressure dressing with a sponge rubber pad was applied. The sac was generally found to be obliterated after the lapse of 5 or 7 days. Fourteen out of 15 patients with chronic olecranon bursitis thus treated were cured, although one has developed a recurrent effusion which requires secondary treatment. Ten out of 11 patients with prepatellar bursitis were apparently cured and obliteration of the sac was effected in one case of popliteal bursitis. Before the treatment was carried out communication of the bursal sac with the knee joint was precluded by the making of aspiration tests.

Copeman, W. S. C. (1943) *Brit. med. J.*, **2**, 263.

Cottrell, J. C. (1944) *J. Amer. med. Ass.*, **124**, 81.

Keiser, D. (1943) *Schweiz. med. Wschr.*, **73**, 1512.

FILARIASIS

See also B.E.M.P., Vol. V, p. 301; and Cumulative Supplement, Key Nos. 490–495.

Definition and classification

Review of all types

Filaria in the American Forces.—The incidence of filariasis among the Forces in the South Pacific zone during 1943–4 is commented upon by Faust who discusses the aetiology, distribution and general features of various types of filarial infection. The filarial organisms which give rise to clinical manifestations are *Loa loa*, *Onchocerca volvulus*, and *Wuchereria bancrofti* and *Filaria malayi*, the two last-named being the most important clinically. In each type transmission to the human host occurs through blood-sucking insects, notably the mosquito. There may be no obvious signs or symptoms of infection for some years, but acute attacks of filarial lymphangitis have been observed among the United States Marines after a short residence of from 3 to 6 months in the Samoan area. In this epidemic the acute stage was in some instances non-pyrexial, and the sites of acute lymphadenopathy were not always those usually involved; it occurred in many different areas of the subcutaneous tissue, with fugitive lesions. In suspected cases of lymphangitis the diagnosis depends upon the finding of microfilariae (pre-larval stage) in peripheral blood (it is usually desirable to make thick blood films) or upon radiological evidence of calcified granules in the lesions. Treatment consists mainly in enucleation of the adolescent or mature worms, at the end of the acute stage of the infection, and in the use of tight bandages applied round the lower limbs in order to prevent excessive swelling. Prevention is a matter of general hygiene and control of contacts with native populations and their mosquito-infested domestic premises.

Faust, E. C. (1944) *Northw. Med.*, *Seattle*, **43**, 9.

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

See also B.E.M.P., Vol. V, p. 334; and Cumulative Supplement, Key Nos. 503–512.

Abnormal conditions occurring in living foetus

Skin

Erythrodermia desquamativa (Leiner's disease).—Sano describes an infantile skin affection which he tentatively classifies as Leiner's disease. He discusses the relation of Ritter's disease, Leiner's disease and pemphigus neonatorum and their possible endocrine origin. Local hyperaemia which proceeds to the formation of bullae and to exfoliation and the presence of Nikolsky's sign have been held to differentiate Ritter's disease from Leiner's disease with its characteristics of cutaneous hyperaemia, desquamation, seborrhoeic scalp, diarrhoea and vomiting and negative Nikolsky's sign. When slight pressure on apparently normal skin separates the upper layers of the epidermis the separation arises from diminished adhesion of the stratum corneum to subadjacent layers and constitutes Nikolsky's sign. The postulated two diseases overlap. The acute intestinal congestion which is consistently found in Leiner's disease appears to be comparable to the gastro-intestinal ulceration described as found in Ritter's disease. Dilatation and hypertrophy of the cutaneous vessels, myocardosis and fatty degeneration of the liver are common to both diseases. In Sano's case, observations which would have correlated the mother's condition during pregnancy to the infant's at birth are lacking, but phenomena observed during the infant's 3 weeks of life and at necropsy

suggest that there was endocrine deficiency in one or in both patients. In the infant's blood calcium and phosphorus were deficient and there was maldevelopment, possibly significant, of the parathyroid glands. Hypocalcaemia with intestinal disorder inhibits vitamin absorption, and would perhaps explain the pulmonary oedema and haemorrhages and the oedematous, not organic, pyloric stenosis which were found at necropsy. Fatty cells in the skin, in the lymphatic and adrenal glands and in the lungs indicated disordered lipid metabolism. An increased glandular layer of the adrenal cortex accompanied a decreased fascicular layer. Good results in previous cases have been claimed from administration of cod-liver oil, riboflavine and staphylococcal vaccines and from diets of high protein with low fat and carbohydrate values.

Digestive system

Congenital atresia of the duodenum.—The importance of close observation of the new-born infant is demonstrated by 2 cases of congenital atresia of the duodenum and ileum respectively in which the patients were treated successfully by operation. The cases are reported by Miller, Greengard, Raycraft and McFadden. In duodenal atresia vomiting is the outstanding symptom. It begins almost immediately after birth and is progressive; the vomit contains bile. The lower part of the abdomen is comparatively flat and the epigastrium is prominent and often shows peristaltic waves. The diagnosis is confirmed by a plain X-ray examination which shows the distended stomach and duodenum and no gas lower in the bowel. Congenital atresia of the ileum is usually situated low down. The vomiting begins immediately after birth and the vomit consists at first of stomach contents, then contains bile and lastly becomes brown and faecal. The entire abdomen becomes distended. X-ray examination shows distended loops of small bowel and no gas in the colon. In both types very early diagnosis and treatment are essential. Before operation the stomach should be emptied by tube, and adequate infusions of saline and glucose and perhaps a little blood should be given. The operation, which is performed under local anaesthesia, consists in lateral anastomosis, the form depending upon the site of the obstruction.

Genito-urinary system

Hermaphroditism.—The clinical problems of hermaphroditism are discussed by Bettinger. An account is given of a female hermaphrodite who underwent surgical extirpation of male gonads, and subsequently married after treatment by oestrogen administration and the dilatation of a rudimentary vagina. There was no uterus or ovarian vestiges. The marriage has proved satisfactory although the patient regrets she cannot have children. The usual clear-cut sex distinctions in different individuals result from a constant difference in the male and female factors in the chromosomes of the gametes, but if during successive generations the genetic sex differences become quantitatively reduced, some degree of intersexuality results. In the higher animals and in human beings sex hormones also play a part in the control of functions during early stages of development. Goldschmidt suggests that male pseudo-hermaphrodites and true hermaphrodites are female intersexes which show sex reversal, whereas female pseudo-hermaphrodites are genetically normal females with virilism due to hormone disturbances. Witschi suggests that male pseudo-hermaphroditism is of two types and may be due to hormonal influences or to partial genetic sex reversal. Moszkowicz has classified all types of intersexuality including borderline conditions such as hypospadias and homosexuality. Plastic operations should be avoided in children and a final decision of sex should be postponed until after puberty.

Bettinger, H. F. (1944) *Surg. Gynec. Obstet.*, **78**, 91.

Miller, E. M., Greengard, J., Raycraft, W. B., and McFadden, Irma (1943) *Amer. J. Dis. Child.*, **66**, 272.

Sano, M. E. (1943) *J. Pediat.*, **23**, 280.

FOOD

See also B.E.M.P., Vol. V, p. 388; and Cumulative Supplement, Key Nos. 513–518.

Vitamins

Source of protectives

The individual ration of milk, cheese, butter, margarine and meat with vegetables should be consumed for its protective value throughout the year. In hot weather, according to Simmonds, meals should be light and generally cold. Points should be expended on tinned fish, pulses and fruits. Increased fluid intake is essential for every age. The addition of bottled fruit juices, although without vitamin value, encourages consumption of water and disguises high chlorination. For heavy workers the addition of half-strength physiological saline solution to watery drinks is judicious; chilling improves most fluids. Articles generally regarded as innutritious are not negligible. Dried and skimmed milk, although devoid of fat and vitamin A, provide protein, calcium and riboflavine. Water contains calcium, and tea, riboflavine. Lean meat and meat extracts offer the vitamin B complex, as does beer, with calcium in addition. Carrots are rich in vitamin A and Brussels sprouts in vitamin C. These vitamins are advantageously combined in turnip tops, spinach, spring greens, parsley and watercress. Cold soup or salad, a hot meat dish and a cold sweet are suitable for the one hot meal usually expected. Sausages, unpopular in hot weather, regain popularity when they are converted into rissoles and served cold with salad. Fish steamed and chilled, with mayonnaise

sauce made of dried egg, and tinned fish are both excellent with salad. Most fish are palatable if soured in vinegar. Dried egg can be the basis of satisfactory omelettes and savouries. Grated raw carrot swells the bulk of stewed fruit without being noticeable. Sandwiches of infinite variety are convenient for meals in the open air and may be made as nutritious as the ordinary cooked meal.

The availability of certain food constituents

Available iron

Sodium phytate and the absorption of iron.—McCance, Edgcombe and Widdowson describe experiments the aim of which was to answer the question whether or not sodium phytate in a diet depresses the absorption of iron contained in that diet but not previously combined with phytate. Nine individuals served as subjects for experiment. For each it was necessary to determine a baseline from which curves of fluctuation in serum-iron could be plotted. The average fasting level in each subject served as that baseline. Estimates were made weekly over a period of from 4 to 8 weeks. Each subject when he arrived in the morning after the overnight fast gave the necessary blood. A breakfast was then taken consisting of bread, jam and ferrous or ferric ammonium sulphate. Blood was taken after 2, 4 and 7 hours from which was determined the rise in serum-iron. To the subsequent breakfasts sodium phytate was added in such proportion that twice as much phytic acid phosphorus was present as would combine with all iron ingested. Estimations were then made illustrating the effect of phytic acid and the findings are given. The experiments illustrate the wide variations in serum-iron content. They show that the ingestion of iron salts raises the serum-iron level and more with ferrous than with ferric salts. The incorporation of sodium phytate diminishes but does not completely inhibit this rise. The inhibition of ferric salts exceeds that of ferrous salts.

Food requirements and intakes

Minimum and optimum requirements

Dietary consultations.—A study of the effectiveness of consultation on diet in the correction of poor dietary habits was undertaken by Kelly and Sheppard. Adult patients to the number of 85 were selected at random and the prevalence of dietary deficiencies was compared before and after advice on correction had been given. A history of food habits, dislikes, intolerances and cravings was taken and each patient was instructed to record his weekly food intake at two different periods, namely before consultation and after it. The dietary records were computed to determine their values in calories, protein, vitamins, minerals, phosphorus, acid-base, fibre and water. The quantities of fats and carbohydrates were not included because the Food and Nutrition Board of the National Research Council of the United States of America has not recommended optimum daily allowances for these foods. It was noted that patients who wished to gain weight were more cooperative in making use of advice. The various reasons why some patients did not eat enough of the essential foodstuffs included ignorance, allergy, indigestibility of certain food items, constipating or laxative effects of foods, adherence to fads and so on. In all but 8 cases the dietary pattern was improved after consultation. In spite of a second interview however there were still many dietary deficiencies shown although they had decreased considerably. The authors recommend consultations on diet to assist in the adoption of a good basic diet and in the substitution of good food habits for bad.

Dietary errors in New Zealand families.—McLaughlin reports a dietary study of 63 urban families in New Zealand representing 277 people and with the wage-earner on the basic wage. Housewives who had given accurate records to the Social Science Research Bureau Survey cooperated. The weekly food consumption was noted by the use of the inventory method, and an estimate was made of kitchen and table waste. The dietaries examined were rarely below standard in energy value. New Zealand families, as compared with typical American families, get more calories from meat and eggs, and less from fruit and vegetables. In general, the more the energy derived from fruit and vegetables the more will the diet cost. Sufficient total protein was usually taken, but about a quarter of the number of people studied did not take the optimum amount of animal protein. Half the number got less than the standard calcium intake. Phosphorus was seldom lacking, but about one-fifth of the number of persons did not get sufficient iron. Some 60 per cent of families had diets below standard in at least one of these factors—energy value, protein, calcium, phosphorus, and iron. There was a sufficient intake of vitamin A and vitamin C, but a lack of vitamin B₁, riboflavin or nicotinic acid. The families were very dependent upon sunlight for the purpose of getting enough vitamin D. The food consumption of the average person studied differed very much from the recommended amounts; more meat and butter was eaten but less cheese, milk, eggs and unrefined cereals. Only about 40 per cent of the families had dietaries adequate in all respects, but as it is possible to obtain sufficient food in order to be well above the recognized standards at a cost lower than that of the average family diet in this survey, it was a matter of choice of foods rather than one of inadequate spending power.

Vitamins

Investigation of excretion of vitamin C.—The theory that faulty proportions of nutrients in the diet, as well as absolute lack, may lead to signs of a deficiency disease has been investigated experimentally by Patterson and Bourquin. The subjects of the study were 8 women engaged in academic work. Ascorbic acid excretion on various diets was estimated. At first 4 standard diets were used, all containing equal quantities of meat and lacking ascorbic acid: a normal, a high carbohydrate, a high fat and a high protein diet. Each diet was given for two separate

periods, during the second of which ascorbic acid was added and the saturation level determined. These 4 diets were used for 2 subjects only. In one of them it was found that ascorbic acid excretion was significantly increased when either the high fat or the high protein diet, especially the latter, was taken. In both, saturation took one day longer on the high protein than on any other diet. For the remaining 6 subjects only the normal and the high protein diets were used. The difference in ascorbic acid excretion was under 2 per cent. In 4 of the 6 subjects the amount of ascorbic acid required for saturation was somewhat increased on the high protein diet.

Urinary excretion of vitamin C.—Evans and Eames survey the urinary vitamin C excretion of various groups of people in Caernarvon. According to Harris's standards, the optimum intake of vitamin C gives a urinary excretion of 2.5 milligrams per 100 cubic centimetres of urine, the normal intake gives an excretion of 2 milligrams and the minimum requirement will give an excretion of 1 milligram per 100 cubic centimetres of urine. In 120 apparently healthy adults the average excretion was 1.4 milligrams, but in 20 of these adults the excretion was below 1. In 124 apparently healthy children under 11 years of age the average excretion was 0.85. Youths of 17 years of age from good homes reached the optimum level. A group of 120 persons with minor ailments such as lassitude and debility gave an average excretion of 0.75. In 195 invalids with major disease the average excretion was 0.55 milligram per 100 cubic centimetres of urine. The lowest excretions were found in rheumatoid arthritis, fibrositis, achlorhydric anaemia, diabetes mellitus, *Bacillus coli* infections and nephritis. Of the apparently healthy children, 22 per cent excreted less than 0.5 milligram of ascorbic acid per 100 cubic centimetres of urine; the authors suggest that discovery of and attention to this class would eliminate much ill health, particularly tuberculosis, in later life.

Evans, G., and Eames, R. O. (1944) *Med. Pr.*, **211**, 184.

Kelly, H. T., and Sheppard, Myrtle (1943) *New Engl. J. Med.*, **229**, 536.

McCance, R. A., Edgecombe, C. N., and Widdowson, E. M. (1943) *Lancet*, **2**, 126.

McLaughlin, F. C. G. (1943) *N.Z. med. J.*, **42**, 155.

Patterson, Isabel, and Bourquin, Anne (1943) *Amer. J. digest. Dis.*, **10**, 390.

Simmonds, Rose M. (1944) *Practitioner*, **152**, 370.

FOOT, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. V, p. 412; and Cumulative Supplement, Key Nos. 520–527.

Infections

Acute infections

Superficial infections.—To a symposium on cutaneous disorders of the foot, Madden contributes a paper on inflammatory disorders. He emphasizes the necessity for careful examination and accurate diagnosis, and says that there is a tendency for doctors as well as the public to attribute all skin disorders of the foot to fungous infections, because they make the diagnosis without microscopical examination of scrapings or cultures from the cutaneous lesions or their contents. In order to prevent inflammation, proper care of the feet is necessary; frequent washing and careful drying, especially between the toes, changing of socks and stockings and suitable, well fitting shoes are required. Much harm is done by application of unsuitable and too strong medicaments such as phenol and camphor, tincture of iodine and formaldehyde. Constitutional factors, for example obesity and excessive sweating, influence the tendency to inflammation. The most common inflammatory disorder is contact dermatitis. Next in importance come pyogenic infections after various injuries. Special types occur in desert warfare, in which the conditions prevent healing. Folliculitis, due to oil, is frequently found in mechanics and others whose shoes become oil soaked. Madden recommends a new treatment for psoriasis by the administration of pancreatin in 5-grain tablets, 4 times a day by mouth, in combination with a scaling ointment. Radiodermatitis is specially dangerous on the feet, because of constant trauma and of the possible development of cancer.

Madden, J. F. (1944) *J. Amer. med. Ass.*, **124**, 743.

FROST-BITE AND TRENCH-FOOT

See also B.E.M.P., Vol. V, p. 440; and Cumulative Supplement, Key No. 528.

Clinical picture

High altitude frost-bite

Comparison with ordinary frost-bite and immersion foot.—Davis, Scarff, Rogers and Dickinson contrast high altitude frost-bite, from brief exposure to intense cold, with the frost-bite and immersion foot of ground Forces and seamen from prolonged exposure to lesser cold. The airman who removes his gloves for a moment incurs a mild type of frost-bite which is shown in fingers waxy white, insensitive, board-like and incapable of flexion active or passive. The condition persists for many hours after the individual's removal to a warmer environment, and paraesthesia may last for weeks; recovery however is complete. The severe type of exposure to cold is divisible into wet and dry varieties. In the wet variety multiple blisters coalesce to form very large blisters on the dorsum of a finger or of the hand. The skin, which

dries after about 3 days, sloughs as a cast of the part and subungual haemorrhages cause loss of the nails. Epithelium regenerates from the remnants of sweat glands and the skin may take more than 10 months to recover completely. In the dry variety, beneath a tense skin, having the appearance of ground glass, the deeper tissues darken from grey to black and mummification proceeds from distal to proximal phalanx. Demarcation from vital tissue is sharply defined within 3 weeks. A striking and inexplicable feature of high altitude frost-bite is that severe cold may cause spontaneous amputation of the affected fingers but may not have any effect on the face exposed to the same degree of cold. In all types the pathological basis is spasm of the peripheral arterioles and endothelial damage in the terminal capillary loops. From this proceeds the extravasation and blistering of the wet type; if firm thrombosis develops at the arteriocapillary junctions before release of vasospasm, dry gangrene ensues. Treatment aims at ultimate relaxation of vasoconstriction but whereas the use of Greene's refrigerator postpones this release by maintaining the extremity at a temperature of between 2° C. and 5° C. for some days, the authors prefer to expose the damaged parts immediately to room temperature; they have found this procedure to be less painful and equally successful. Vasodilator drugs are inert in high altitude frost-bite.

Davis, L., Scarff, J. E., Rogers, N., and Dickinson, M. (1943) *Surg. Gynec. Obstet.*, 77, 561.

FUNGOUS DISEASES

See also B.E.M.P., Vol. V, p. 448; Interim Supplement, No. 13*; and Cumulative Supplement, Key Nos. 529-544.

Dermatophytides

Aetiology and clinical picture

Industrial cases.—Downing considers the superficial lesions of fungous infection in relation to occupational dermatitis. Microsporiasis produces ringed, scaly patches and *Epidermophyton* attacks macerated skin, as does *Trichophyton endothrix*. *Trichophyton ectothrix* produces severer inflammatory reactions and *Monilia albicans* affects moist flexures of the skin. Secondary fungous infection of an industrial dermatitis is unusual; 14 instances occurred in 406 cases. Distant fungous infections however may sensitize the skin elsewhere. The lesions, devoid of fungi, which occur in such sensitized areas are called dermatophytides; they originate from mechanical and chemical industrial contacts. An instance is provided by 20 workmen who were affected by manual dermatitis due to wearing leather gloves which were saturated with soap chips and glycerin. In every case there was an accompanying fungous infection of the feet. Investigations among plate printers, and among operatives who had contact with torch oil, who were suffering simultaneously from dermatophytosis and dermatitis, suggest cause and effect but are not proof positive, since a primary irritant is independent of predisposing factors and dermatophytosis is widespread among workers, whether affected or unaffected by dermatitis. Legally dermatophytosis does not provide a basis for a claim for compensation unless it is proved to result from, to be grafted on or to be aggravated by trauma originating at work. In order to distinguish mycotic infections from occupational dermatitis, the history of the case, with scrapings and patch tests and clinical experience are essential. In the treatment of a vesicular dermatitis, boracic and calamine lotions and zinc ointment, later with tar, make a suitable sequence, occasionally with X-ray irradiation. Dermatophytosis responds to soaking in a solution of potassium permanganate, after which boric acid, salicylic acid and sulphur may be used in ointment and powder. Sulphonamides, orally or locally, are unsuitable.

Treatment

Chlorophyll in dermatophytosis of the feet.—Wallace, Day and Moorman report on the effect of chlorophyll ointment on dermatophytosis of the feet and similar lesions, in students. The ointment was composed of finely ground water-soluble magnesium (or copper) chlorophyllin 1 gramme in hydrous wool fat 28 grammes. In some cases a small amount of water was added to aid mixture. After the ointment had been mixed well, it was autoclaved and was then ready for use. A thin layer of ointment was applied once daily and massaged in lightly during 4 or 5 weeks. Improvement was obtained in 22 of 31 cases. Of the 17 cases in which *Trichophyton* was isolated, 4 improved and fungi were not isolated from later cultures, 9 improved but the fungi were still isolated from cultures and in 4 there was no improvement and fungi persisted in cultures. Of 14 cases in which the disease was possibly caused by staphylococci, 9 showed improvement although the organisms persisted in cultures. Further clinical observation was made several months after treatment had been stopped. Almost invariably the original condition had recurred. The ointment was non-irritant and gave quick relief from itching. It seems that chlorophyll does not actually reach the source of the infection, and that it has no appreciable bactericidal or bacteriostatic action. It has been suggested that the action of chlorophyll is due to its ability to increase the resistance of tissue cells by some physico-chemical process.

Downing, J. G. (1944) *J. Amer. med. Ass.*, 125, 196.

Wallace, G. I., Day, J. K., and Moorman, H. E. (1944) *Arch. Derm. Syph.*, N.Y., 49, 128.

GALL-BLADDER AND BILE-DUCTS

See also B.E.M.P., Vol. V, p. 477; and Interim Supplement, No. 11*.

Cholecystitis*Treatment*

Importance of diet.—In a paper on the prevention and treatment of cholecystitis and cholelithiasis, Davidson first discusses the physiology of bile formation. The aetiology of cholecystitis and gall-stones is still obscure and authorities differ in their estimation of the relative importance of different factors, but it has been proved that the incidence is greatest in women over 40 and that a sedentary life and unbalanced diet, which cause obesity, are important. Cholecystitis also occurs in or after acute general infections, such as typhoid fever, and may be followed later by gall-stones. The part played by micro-organisms of various kinds in the formation of the latter, and their sources of origin and route to the gall-bladder, are matters of controversy. The single 'pure' cholesterol stone is probably the result of a metabolic defect, whereas the origin of the multiple faceted cholesterol-pigment-calcium stones is closely associated with infection. Although treatment is often necessarily surgical, medical measures are required in acute cholecystitis without calculus in the pre-operation phase, or when operation is contra-indicated. Failing the relief of pain by the antispasmodics—the nitrites and theophylline with ethylenediamine—from $\frac{1}{4}$ to $\frac{1}{2}$ grain of morphine may be given hypodermically; water and glucose should be given by the mouth and, on the assumption of an infective factor, the administration of sulphathiazole or sulphadiazine should be started at once. Later, biliary drainage may be improved by means of suitable diet. Fats and protein products promote the flow of bile, and the natural fats such as butter, milk and cream and the yolk of eggs are well tolerated in limited quantities, but fried foods and indigestible types of fatty food should not be given. Fat content and cholesterol content are not consistently correlated and some foods must be eliminated because of the latter only; brains and sweetbread show the most important excess of cholesterol in comparison with fat. The aids to gall-bladder activity are magnesium sulphate and a strong solution of peptone. Atropine and the barbiturates relieve spasm, alkalis or acids may be given as indicated, and olive oil, given before meals, relieves dyspepsia and flatulence in many cases. Bile-salts, the most effective choleric agents known, may be given as the sodium salt of dehydrocholic acid, which is obtainable as decholin and dehydrocholin.

Post-operative treatment

Effect of complications.—Macdonald discusses the principal factors involved in the incidence of symptoms after cholecystectomy and states that such symptoms are not given adequate attention. Their pre-operative consideration is of primary importance. Correct diagnosis of post-operative conditions should not be difficult but treatment may be. The percentage of patients who are not cured by cholecystectomy varies from 15 to 35 per cent; in 90 per cent of patients with calculus disease good results are obtained but in non-calculus cases the percentage of patients showing results is much lower. Surgical treatment should therefore be undertaken only after profound consideration because the main symptom-producing mechanisms, namely hepatitis, cholangitis, common duct disease, pylorospasm or sphincter spasm and so on, are not removed by cholecystectomy. Many patients with non-calculus disease of the biliary tract receive symptomatic relief with medical treatment and it is obviously better to effect improvement by medical means than to get poor or fatal results by surgical methods. Post-cholecystectomy symptoms are discussed under the headings of the main aetiological factors. These are (1) wrong diagnosis, (2) residual disease, (3) common duct calculi, (4) common duct stricture, (5) partial obstruction of the duodenum or ductal system, (6) functional changes, (7) lack of or indifference to medical treatment, (8) traumatic neuroma in the wound and (9) malignancy. A small number of patients have post-operative symptoms of varying severity and of major or minor importance but these generally subside after a short period. The longer after operation symptoms occur and the longer they last the more likely are they to be organic in origin. The major post-operative conditions are reviewed. The author considers that in many instances their incidence can and should be reduced.

Carcinoma of gall-bladder*Clinical picture*

In 77 surgical cases of carcinoma of the gall-bladder Vadheim, Gray and Dockerty analyse the pathological and clinical data. They state that the gall-bladder is the most usual site of carcinoma of the biliary passages. It occurs most frequently in women from the age of 60 years onwards. Pre-existent stones may be possible precursors of carcinoma because of the inflammation they cause. In the authors' series early symptoms were colicky pains or gaseous dyspepsia or, more rarely, symptoms which were not referable to the gall-bladder. When carcinoma supervened the symptoms became mainly pain or loss of weight, dyspepsia, weakness, anorexia, constipation, nausea and vomiting. Steady pain varied from mild to acute, generally in right upper quadrant of the abdomen and sometimes extended into the back or the right shoulder. Loss of weight may occur in cholecystitis but is more common with early carcinoma of the gall-bladder. A palpable tumour was present in 40 per cent of the authors' cases. Increased leucocytosis was usually found in patients with recent cholecystitis. Haemoglobin was well over 75 per cent in many of the cases. The diagnosis of carcinoma was in no case made as a result of X-ray examination. The wall of the gall-bladder was usually

thickened with papillary ingrowths. In 54 per cent of patients the point of origin was in or near the fundus. Metastases were often found—in the liver, regional nodes, pancreas, omentum and ovaries. Sixty-four of the 77 cases were cases of adenocarcinoma; there were also 2 cases of squamous-celled carcinoma, in which usually the grade of malignancy is low. Squamous metaplasia was found in some of these cases and thus gave evidence of the metaplastic theory of origin of squamous-celled carcinoma. Perivascular and intravascular spread were found. Carcinoma may also spread along the nerve sheaths of the gall-bladder. In the authors' patients in whom pain and wasting were noteworthy features the growth had extended beyond the gall-bladder. In carcinoma, grade I, 5-year cures were obtained in 45 per cent of the cases, in 4.3 per cent in cases of grade 2 and in none of the other grades.

Davidson, L. S. P. (1944) *Edinb. med. J.*, **51**, 184.

Macdonald, D. (1943) *Amer. J. Surg.*, N.S., **62**, 19.

Vadheim, J. L., Gray, H. K., and Dockerty, M. B. (1944) *Amer. J. Surg. N.S.*, **68**, 173.

GARGOYLISM

See also B.E.M.P., Vol. V, p. 496.

Clinical picture

Incidence in two brothers

The condition known as gargoylism derives its name from the enlarged retracted head, flattened nose, deformed limbs and abnormal posture with all joints slightly flexed, which give the subject a grotesque appearance. Lurie and Levy state that it has been established that the condition is of familial and congenital origin and that it is usually not obvious until the second year of life. They describe the affection in two brothers of healthy and not consanguineous parentage. The underlying pathological condition is a cartilaginous maldevelopment and a lipid deposit in the reticulo-endothelial cells, brain, cornea, liver, spleen and pituitary and lymph glands—hence the alternative name of lipochoondrodysplasia. In the authors' patients there was mental retardation which started at the age of 4 years, helplessness and poor memory. The hearing was deficient. Skeletally the noteworthy degenerations in both patients comprised rounding of the anterior margins of the vertebrae with absorption in the lumbar region which caused kyphoscoliosis; this condition was observed at the age of 17 months as the first abnormality in the older boy. In both children the cephalic sutures were closed, ossification was delayed and the teeth were spaced and peg-shaped. The sphenoid bone was enlarged but the increased size of the sella turcica was proportional only to the general cephalic enlargement. The height of both boys was below the ordinary standard for their ages; the weight was somewhat in excess but there was not gross adiposity. The hair of the head was coarse and dry and the back and extremities were unduly hirsute; the skin was dry and roughened. The thyroid gland was not enlarged. The liver and spleen were enlarged, the genitals were small and the testes were arrested within the external abdominal rings, which were widely patent, as was the umbilical ring. With the exception of findings in plasma bilirubin, phosphatase and protein and in hippuric acid excretion which all indicated liver damage, laboratory tests proved to be uninformative. Corneal clouding, which in 75 per cent of cases of gargoylism is present, was in these instances absent. Gargoylism is a lipidosis distinct from Morquio's disease in which joint movement is free and the intellect unclouded.

Lurie, A. L., and Levy, S. (1944) *Amer. J. med. Sci.*, **207**, 184.

GASSING AND POISON GASES IN WAR

See also B.E.M.P., Vol. V, p. 502; and Cumulative Supplement, Key Nos. 552–557.

Lung irritant (asphyxiant) gases

Physical signs

Acute phosgene poisoning: radiology of chest.—Captain Sage, of the United States Medical Corps, reports the radiological appearances of the chest in a case of acute phosgene poisoning in a man aged 28 years, a member of the Chemical Warfare Service. The outstanding pathological feature in the lungs in phosgene poisoning is pulmonary oedema. This was well shown by serial skiagrams in this case. The first film, taken 22 hours after exposure, showed diffuse soft mottled infiltration and thickening of the lung markings. As early as 70 hours after exposure the appearances were lessening in intensity; at the end of 7 days the lungs had cleared except at the left base, where there was some residual infiltration. Six weeks after exposure the patient's radiological appearances were normal, and lipidol study showed no changes in the visualized bronchial tree. This is of considerable interest as it has been claimed that residual damage to the lungs occurs in some cases. Secondary changes may be demonstrable at a later date. Other gases likely to produce similar changes in chest skiagrams are the lung irritants: chlorine, diposgene, nitric oxide and chloropicrin. Different physical properties in some gases may however result in different pathological changes.

Sage, H. H. (1944) *Amer. J. Roentgenol.*, **51**, 9.

GLANDULAR FEVER

See also B.E.M.P., Vol. V, p. 559.

Aetiology

Listeria monocytogenes

Report of a third case.—Webb gives an account of a case of glandular fever (infectious mononucleosis) in a man aged 20 years, a medical student at Cambridge University. There was an acute febrile onset and the fever lasted for 11 days. After a brief period of normal temperature there was a relapse of the symptoms of glandular fever and on the fourteenth day after onset the patient showed a typical leucocyte count, namely 87 per cent of total mononuclears. The case is the third of its kind reported to be due to the same infective agent, namely *Listeria monocytogenes*, which was first isolated by Murray, Webb and Swann. Pons and Julianelle later reported the isolation of *L. monocytogenes* from venous blood. Pirie had proposed the term *Listerella* for the parasite of glandular fever but at the third International Congress of Microbiology held in New York the name *Listerella* was disallowed as it had been applied to a mycetozoon by Jahn in 1906 and the name was changed to *Listeria*. Webb refers to articles ascribing the causal factor of glandular fever to *Listeria monocytogenes* by workers in East Anglia, in the Eastern seaboard of the United States of America and in Copenhagen but cautiously adds that the part played by *L. monocytogenes* is still open to question because it has not yet been confirmed by a sufficient number of cases to justify its acceptance as the sole possible agent responsible for glandular fever. It has also been suggested that the infection may be caused by a virus.

Webb, R. A. (1943) *Lancet*, 2, 5.

GLAUCOMA

See also B.E.M.P., Vol. V, p. 575; Interim Supplement, No. 18*; and Cumulative Supplement, Key Nos. 562–565.

Secondary glaucoma

Aetiology and pathology

Association with capillary angioma of face.—Glaucoma associated with naevus flammeus (capillary angioma) of the face is reported by Alvis and Toland. A boy, 14 years of age, gave a year's history of dimness of vision in the right eye. He had a naevus flammeus involving an area corresponding to the distribution of the ophthalmic and maxillary branches of the right trigeminal nerve to the skin and to the mucosa of the nose and throat. The tension in the right eye was 43 millimetres Hg (Schiötz), in the left eye 16 millimetres; vision was 6/12 and 6/6 respectively. Perimetric examination revealed an enlarged blindspot on the right with slight contraction of the field in all diameters. Ophthalmoscopic examination showed deep cupping of the optic disk; the vessels were pushed to the nasal side. Pilocarpine reduced the tension in the affected eye to 30 millimetres. Improvement however was only temporary and a month later trephining was done. The tension remained normal for 10 months and then rose; drugs controlled it for 6 months. It then rose again and perforating cyclodiathermy was performed in two stages. Nervoid tissue was found on the sclera and coagulated with the diathermy terminal. The authors hold that the vascular anomaly was responsible for an abnormal circulation in the globe.

Primary glaucoma

Aetiology

Blood cholesterinase theory disproved.—Rados has studied the blood cholesterinase values of patients with glaucoma. The method of estimation used was a modification of that of Ammon, whereby the amount of carbon dioxide liberated from a sodium bicarbonate solution by the acetic acid resulting from hydrolysis of acetylcholine is measured. By this the amount of cholesterinase is indicated. Results are expressed in cubic millimetres of carbon dioxide liberated from 7.5 milligrams of acetylcholine chloride in 1.5 cubic centimetres of sodium bicarbonate (Ringer's) solution by 0.5 cubic centimetre of serum diluted 50 times with this solution. Normal values are given by two authorities as 60 to 100 cubic millimetres and 40 to 120 cubic millimetres respectively. Of 61 patients with glaucoma, many of whom were examined repeatedly, 59 had blood cholesterinase values between 40 and 120, that is within the limits of normal. Two patients only gave figures respectively above and below the normal range. Of 12 patients with acute glaucoma all had values towards the upper limit of the normal. These findings do not offer any support to the theory that excessive destruction of cholinergic substances in the eye, consequent upon an abnormally high concentration of cholesterinase in the blood, is a prime factor in glaucoma.

Treatment

Chronic glaucoma: iridencleisis.—Evans, in a note on iridencleisis, states that the best results are obtained in non-congestive glaucoma, chronic or subacute. The author recommends a modification consisting in total section of the temporal pillar of the withdrawn iris and its reposition into the anterior chamber, the nasal pillar being retained for inclusion through the lips of the incision. This modification is suitable when the iris can be easily withdrawn. Peripheral iridectomy is performed by oblique incision of the withdrawn iris, only the outer two-thirds being cut. The iris is replaced by pressure while the tongue of tissue is held in the wound.

Chronic glaucoma: the Lagrange operation.—Smith supplies a few technical hints in order to facilitate the performance of the Lagrange operation for glaucoma. The position of seizure

of the globe for fixation is best controlled by a scleral stitch. The head must be sufficiently dependent. The iridectomy should be a 'buttonhole' one unless the patient is very old or cataract or sclerosis of the lens is present. The repositor should always be used to ensure that no impaction of the iris occurs at the angles of the wound, which should not exceed 6 millimetres in width. The sclerectomy should be about 1.5 millimetres from the limbus.

Furmethide compared with mecholyl.—Since 1939 mecholyl (acetyl- β -methylcholine chloride) with prostigmin has rivalled pilocarpine and eserine in the treatment of primary acute glaucoma. Uhler compares furmethide (furfuryltrimethylammonium iodide), introduced in 1941, with mecholyl. A tension of less than 35 millimetres Hg measured by the Schiötz tonometer is a relatively safe pre-operative level. One drop of 10 per cent furmethide was instilled into the conjunctival sac every 15 minutes during a period of 2 hours, then every 3 hours until tension was normal or operation was performed. Of 23 patients considered, in 69 per cent the tension was reduced to one of 35 millimetres Hg or less. Of those previously receiving miotics 64 per cent reached this reduction and of those previously untreated, 89 per cent. Of patients with a tension of over 55 millimetres Hg, 60 per cent and of those under 55 millimetres, 87 per cent, experienced this reduction. A field defect of less than 30 degrees in any meridian and a blindspot enlarged not more than 10 degrees in any diameter was denominated early glaucoma. Of such, 67 per cent accomplished this reduction as also did 74 per cent of patients with late glaucoma which comprised all other degrees. Comparison with 43 cases treated with mecholyl showed outstanding difference only in early and late groups; the 92 per cent success of mecholyl in early cases surpasses the 67 per cent of furmethide whereas the 74 per cent success of furmethide in late cases surpasses the 41 per cent of mecholyl. In acute glaucoma secondary to cataract extraction, uveitis and trauma, the two drugs ran parallel. Neither was effective in glaucoma secondary to venous thrombosis. Of 20 patients with chronic glaucoma, uncontrolled by pilocarpine, furmethide produced an initial drop in 15. Furmethide is not permanently reliable.

The need for review of operative methods.—Knighton discusses the question of reoperations in the treatment of glaucoma. They are made necessary by failure of the primary operation, however wisely selected or skilfully performed, to effect a cure. The aetiology and pathology of glaucoma are little understood; the relief of one symptom, hypertension, does not necessarily cure the disease. In 10 per cent of cases hypertension returns and has to be dealt with and the ophthalmic surgeon is faced with the problem of choosing the best way of dealing with the complications which have arisen. Should the same operation be tried again, or should one of a different kind be attempted? Finding little to guide him in the literature towards a solution of the problem, Knighton recounts his own experience of various procedures and their success or failure. During the past 2 years he has personally examined the patient in every case of operative failure which occurred in the Knighton Clinic at the New York Eye and Ear Infirmary, both in an attempt to discover the reason for the failure, and in the hope of finding a simpler remedy than a second extensive operation. He met with a measure of success but concludes that the whole subject deserves more investigation and discussion than it has hitherto received.

Alvis, B. Y., and Toland, V. A. (1943) *Amer. J. Ophthalm.*, **26**, 720.

Evans, P. J. (1943) *Brit. J. Ophthalm.*, **27**, 548.

Knighton, W. S. (1943) *Arch. Ophthalm.*, N.Y., **30**, 499.

Rados, A. (1943) *Arch. Ophthalm.*, N.Y., **30**, 371.

Smith, E. T. (1943) *Med. J. Aust.*, **2**, 211.

Uhler, Ella M. (1943) *Amer. J. Ophthalm.*, **26**, 710.

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also B.E.M.P., Vol. V, p. 599; and Cumulative Supplement, Key Nos. 569–574.

Physiology

Control of function

Effect of pituitary gland extract and other substances.—Means¹, from the Thyroid Clinic of the Massachusetts General Hospital, discusses the physiology of thyroid function, its control by the anterior lobe of the pituitary gland and the action of agents such as iodine, cyanides, cyanates, sulphonamides and thioureas upon the working of the thyroid gland. The iodine storage capacity of the normal thyroid gland has a limit or ceiling and after it is reached the surplus remaining in the blood is excreted. The hyperplastic thyroid gland collects more iodine than does the normal gland. Iodine is released from the gland as a constituent of thyroid hormone and its amount can be estimated by measuring the protein-bound iodine in the blood or by measuring the oxygen consumption of isolated tissues such as mouse liver when acted upon by the plasma. Thyroid hormone controls basal metabolism and also influences growth, differentiation of tissue, distribution and exchange of water salts and colloids in the body, storage of glycogen in the liver, circulation and the nervous system. The pituitary gland acts as governor of the activities of the thyroid gland so as to maintain at the optimum level the concentration of thyroid hormone in the blood. This it does by producing a hormone of its own. The pituitary gland in turn is influenced by thyroid hormone and thus a hormonal balance is maintained—in the words of Salter, 'a pituitary-thyroid axis'. There is also a pituitary-gonadal axis. In addition to the faculty of stimulating thyroid function the pituitary

hormone has gonadotrophic, adrenotrophic and growth-promoting fractions which can be extracted from the hormone, leaving the thyroid stimulant behind. Iodine is stored in the thyroid gland in a protein combination known as iodothyroglobulin, from which the hormone is derived. When the supply of iodine from the food circulating in the blood is scanty the gland hypertrophies. Artificial iodinated proteins have been prepared which have several times the physiological activity of the natural whole gland. An ingenious method of observing the course of iodine metabolism is to use irradiated or tracer iodine, when sections of the gland take their own photomicrographs; in human beings the process can be recorded by means of Geiger counters placed over the gland. Cyanides, cyanates and sulphocyanides lower thyroid hormone production and produce hyperplasia of the gland. Their action can be countered by iodine. Sulphonamides and thioureas have a similar action which can be countered by feeding with actual thyroid substance as in myxoedema, in which thyroid tissue is absent. The origin of Graves's disease probably lies in nervous impulses via the hypothalamus-pituitary route. Treatment with iodine causes involution of the hyperplastic gland and lessens the hyperthyroidism. The mechanism of this action is not yet thoroughly understood.

Toxic goitre

Aetiology

Effect of potassium thiocyanate.—Goitre has been produced in animals by means of many agents including the sulphonamides and potassium thiocyanate; the therapeutic value of the latter makes it necessary to inquire into its effect on the human thyroid gland. Rawson, Hertz and Means twice encountered goitres which developed during the treatment of hypertension with potassium thiocyanate. Hypothyroidism, low basal metabolic rate, low blood iodine, decreased urinary excretion of iodine, increased excretion of thyrotrophic hormone and in one of the cases exophthalmos, were the salient manifestations. The explanation offered by the authors is that physiologically the anterior lobe of the pituitary gland issues a hormone to the thyroid gland. Thus stimulated, the thyroid gland issues its hormone in part to the tissue cells, maintaining the basal metabolic rate, and in part returns it to the pituitary gland in order to control its output of hormone. The administration of thiocyanate imposes a block to the distribution of thyroid hormone. The tissue cells show the effect of this deprivation by a lowered basal metabolic rate and the anterior pituitary lobe, uncontrolled, issues its hormone in excess to the thyroid. The thyroid gland although stimulated to overproduction cannot distribute its product, hence there is a hypertrophy of frustration. The administration of an adequate amount of iodine is essential and Astwood found that iodine administration prevented the development of thiocyanate goitre in animals. Moreover, after the development of goitre, administration of iodine can force the thiocyanate block; thyrotoxicosis then results. Therapeutically in both cases the block was by-passed by the authors by administration of thyroid extract when thiocyanate was employed, thyroid extract (U.S.P.) 0.1 gramme and 0.2 gramme given on alternate days being added to the regimen. Thus the hypertension was controlled and the hypothyroidism nullified and the goitres disappeared.

Influence of pituitary extract.—Means² discusses the nature of Graves's disease, which term he considers more suitable than toxic goitre, as goitre is not always present, or always toxic. He considers that the condition represents a breakdown under stress or strain in a given individual's weakest part. The role of the thyroid stimulating hormone (TSH) of the pituitary gland in the disorder is far from established. It has been observed that this hormone, if exposed as part of a substrate to thyroid cells growing in tissue culture, loses its function, the process being that of inactivation not of degradation since it can be re-activated if it is treated with mild reducing agents. The thyroid gland in cases of thyrotoxicosis has the greatest power in this respect, and the inactivated TSH is excreted in the urine in this form. After the urine is heated considerable thyrotrophic activity develops. In the classic type of case TSH stimulates the thyroid cells and they produce an excess of their hormone, at the same time inactivating the TSH. In the ophthalmoplegic form (exophthalmic ophthalmoplegia) the TSH is not inactivated to the same degree, the production of thyroid hormone is not increased and TSH is excreted in its active as well as its inactive form in the urine; at the same time excess of TSH aggravates the ophthalmic situation. The cause of asymmetric ophthalmic involvement in Graves's disease still eludes explanation. After thyroidectomy the exophthalmos often appears to subside rapidly but actual measurements show it to increase, the apparent decrease being due to decline of lid retraction. In the classic type however the exophthalmos may ultimately decrease but a different picture is seen in the special ophthalmopathic group, in which protrusion increases and is associated with oedema of the lids and conjunctiva and with ophthalmoplegia. Müller's muscle is rudimentary or absent in man and to it cannot be attributed the cause of exophthalmos but the increase of intra-orbital contents is striking and significant. Weakness of the extra-ocular muscles may also play a part in reducing the backward pull upon the eye-ball; the fall in the counteracting tissue pressure then allows a flow of fluid from the capillaries and augments the tendency to proptosis. Considerable evidence is available to support the view that an excess of thyrotrophic hormone has some relation to the ophthalmic pathogenesis but the relation is probably not a simple one.

Treatment

Toxic effects of thiourea.—Newcomb and Deane record a granulopenia apparently due to the toxic effect of thiourea on bone marrow. A woman aged 44 years was admitted to hospital, having an enlarged thyroid with thyrotoxicosis of nervous rather than of cardio-

vascular type. After a week's administration of phenobarbitone (luminal) and bromide, treatment with thiourea was substituted in doses of 1 gramme thrice daily. The total leucocyte count after a fortnight was 9,200 and the differential count was normal. After 10 days the dose was reduced to 1 gramme twice a day and finally to 1 gramme daily, so that 83 grammes were taken in 5 weeks with satisfactory progress except for 4 days of pyrexia from influenza. Suddenly epistaxis and general purpura developed with ulceration of the buccal mucous membrane and bleeding gums. Thiourea administration was forthwith discontinued. The blood count showed erythrocytes 4,500,000, leucocytes 4,100, with 24 per cent of granulocytes and 1,800 platelets. Haemoglobin showed 87 per cent and bleeding time, but not coagulation time, was greatly prolonged. Sternal puncture gave a count in percentages of polymorphonuclear cells 7, lymphocytes 16, myelocytes 44, myeloblasts 10.5, erythroblasts 39, normoblasts 48; platelets were scanty. The many myelocytes justified a good prognosis. A pint of whole blood was infused on the second day after the appearance of purpura with immediate cessation of gingival bleeding. Pyrexia developed after the administration of pentnucleotide (sodium pentose nucleotide) and it was discontinued. The blood counts gradually became normal. In the absence of other drug treatment thiourea appears to be responsible for the toxic effects.

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GONORRHOEA

See also B.E.M.P., Vol. VI, p. 1; Interim Supplement, Nos. 15* and 18*; and Cumulative Supplement, Key Nos. 575–578.

Bacteriology

Resistance to sulphonamides

Laboratory tests of gonococcal strains.—Goodale, Gould, Schwab and Winter describe a simple laboratory method of determining whether a given strain of gonococci is resistant or responsive to sulphonamides. Pure cultures of gonococci having been obtained, 4 subcultures are prepared, one on Mueller-Hinton medium and 3 on the same medium containing sulphathiazole in concentrations equivalent to 0.10, 0.25 and 0.50 milligram per 100 cubic centimetres respectively. The plates are incubated at 36–37° C. for from 18 to 36 hours. Equal or almost equal growth on all 4 plates indicates a sulphonamide-resistant strain. Good growth on the control plate with none, or only traces, on the sulphathiazole plates indicates a susceptible strain. Intermediate results are obtained with partially resistant strains. Of 58 patients studied 22 were classified as resistant, 33 as responsive and 3 as partially resistant. Clinically, all of the first group failed to respond to chemotherapy in less than from 2 to 4 weeks; all of the second group cleared up promptly, most of them within 48 hours. Of the third group, one proved clinically to be of resistant type and the others were intermediate, requiring about a week for cure. The test is useful as a guide to treatment.

Gonorrhoea in males

Complications

Purulent arthritis and suppurative myositis.—Linner reports a case of acute gonorrhoeal urethritis complicated by suppurative myositis and purulent arthritis which at first was treated by small daily doses of sulphathiazole. The anterior urethritis was apparently cured after a fortnight's course of chemotherapy and of daily instillations of potassium permanganate solution into the urethra but 2 days later the patient had pain in the left calf which became very swollen. The left knee also became swollen, stiff, hot and tender. Fluctuation was present and there was ballottement of the patella. Gonococci were cultured from serosanguineous fluid obtained from the calf and the patient was given sulphamethazine; there was not any resultant improvement. The left calf was then incised and successfully drained but the purulent arthritis failed to respond to administration of sulphamethazine or sulphamerazine or to intravenous injections of typhoid vaccine. Penicillin administered intravenously produced only temporary improvement. Penicillin was then injected into the synovial cavity and cultures of the synovial fluid became sterile after the injections had been repeated twice. The case may illustrate the development of resistance to sulphonamide compounds after inadequate doses because the gonococci which were isolated from the calf abscess grew readily on media containing strong concentrations of various sulphonamide derivatives. It is not possible to state whether the strain was originally resistant to sulphonamides or whether it acquired resistance after exposure to low concentrations of sulphamethazine early in the course of treatment. For the treatment of acute gonorrhoeal urethritis it is recommended that 4 grammes of sulphathiazole or sulphadiazine should be given daily for from 5 to 7 days. It is possible that urethral instillations of potassium permanganate may favour the dissemination of gonococcal infection and the formation of metastatic abscesses. The hypertherm cabinet is generally more effective than is typhoid vaccine for artificial fever therapy in resistant cases of gonococcal arthritis.

Treatment

Classification according to duration of disease.—For purposes of treatment male patients

with gonorrhoea are divided by Ballenger, McDonald and Coleman into three groups as follows. (1) Acute cases in which the discharge has been present for under 48 hours, and of which a high percentage of patients can speedily be cured. (2) Cases in which more than 48 hours have elapsed since the discharge started, and in which the chance of cure within 2 weeks is between 80 and 90 per cent. (3) Chronic or recurrent cases, in many of which some complication has developed and which require further investigation before treatment is commenced or recommenced. In group (1) the treatment advised comprises the giving of sulphathiazole by the mouth in doses of 1.5 grammes 4 times a day for the first 2 days, then 1 gramme 4 times a day for a further 2 days; instillations into the anterior urethra are made once a day for 4 days. In carrying out the latter part of the treatment the patient is first instructed to pass urine and the meatus is washed; then 1.5 cubic centimetres of a 5 per cent silver protein solution, freshly prepared each day, are injected into the anterior urethra and retained there with clamps. The meatus is sealed with non-flexile collodion and the clamps are then removed. A condom is put on and the patient is told to hold his urine for 4 hours. All treatment is discontinued at the end of 4 days and the patient is kept under daily observation. If no discharge appears a urethral sound is passed as a provocative test at the end of the second, third and fourth weeks. Failing any return of the discharge the patient is then certified as cured. In group (2) sulphathiazole is recommended in doses of 1 gramme 3 or 4 times a day and instillation treatment is continued. For group (3) a urologist's help is required.

Typhoid vaccine given by intravenous drip.—A method of inducing artificial fever with typhoid vaccine given by intravenous drip is described by Knight, Emory and Flint. The authors attribute the waning of popularity of foreign protein as a means of inducing fever to the inconsistent results and the relatively high incidence of complications, and state that the intravenous drip method of administration overcomes both these drawbacks. They have treated 91 patients, each of whom has received from one to 14 treatments consisting of from 2 to 7 hours' pyrexia. Most of these patients were young adults with resistant gonorrhoea. They were carefully selected according to standards at first a little more strict than, but recently similar to, those used in selecting patients for hyperthermy treatment. The technique is as follows. The patient, wearing only a pyjama jacket, lies under a wooden skeleton frame. This consists of two sides and a top and is 5 feet long, 3 feet wide, 12 inches high at the head end and 10 inches high at the foot. Over the frame the upper bedclothes are placed, hanging down at the head end around the patient's neck. This method avoids the discomfort of perspiration-soaked blankets pressing on the patient, and heat loss is not increased, chiefly because patients are much less restless than those in a hypertherm and do not toss off their coverings. Blood pressure and pulse do not fluctuate so much and patients often sleep through the treatment. The thermometer is kept in the rectum between readings. The typhoid vaccine used is the standard American Army triple vaccine used for prophylactic inoculations. It is measured in a tuberculin syringe and diluted with 5 per cent glucose-saline. The dose is determined by the patient's response; careful watch must be kept on the temperature and blood pressure throughout. In skilled hands the treatment is simple and safe.

Modern methods and the general practitioner.—Osmond¹ surveys the modern treatment of gonorrhoea in the male from the general practitioner's point of view. (1) Bacteriological diagnosis must precede treatment. Only in urgent clinically probable cases should chemotherapy be started while the pathologist's report is awaited. If gonococci are not found the examination should be repeated after the patient has held his urine for at least 4 hours. (2) Before chemotherapy is begun contra-indications must be noted and patients who show them excluded from the treatment. The sulphonamide preparations in order of merit are (1) sulphadiazine, (2) sulphathiazole, (3) sulphapyridine and (4) sulphanilamide. The patient must be seen daily and should not be supplied with more of the drug than will suffice for one day. For the purpose of avoiding haematuria the urine should be made alkaline with a citrate mixture and the total fluid intake for the 24 hours should be not less than 6 pints. The dosage of sulphathiazole recommended is 5 grammes (10 tablets) daily for 2 days, divided as follows: 3 tablets on rising, 2 at midday, 2 at teatime and 3 at bedtime. If the discharge has not stopped at the end of 2 days the same doses should be continued for a further 2 days. If minor signs of urethritis persist irrigations by a skilled person should be given. The urethra is first washed out, then the fluid is allowed to run into the bladder. If after 7 days the patient is not cured a second course of chemotherapy may be given but a complete leucocyte count should first be made in order to avoid the risk of agranulocytosis. The patient should be referred to a specialist if the second course fails or if complications or signs of intolerance appear. In successful cases the patient should be re-examined weekly for 3 weeks and a final examination should be made at the end of 3 months which should include bacteriological tests and urethroscopy; a specimen of blood for a Wassermann test should be taken as well.

Gonorrhoea in adult females

Treatment

Results of penicillin therapy.—Cohn, Studdiford and Grunstein treated with penicillin 42 adult female patients with gonorrhoea, who had proved to be resistant to at least 2 courses of sulphathiazole; 2 further patients who were hypersensitive to sulphonamides were also so treated. Of these patients 43 promptly became bacteriologically negative and remained negative during a period of continued observation. The bacteriological reversal took place

as a rule within 12 hours after termination of therapy. A total of 75,000 Oxford units of penicillin appears to be satisfactory in the treatment of sulphonamide-resistant gonorrhoea in the adult female; the therapy may be completed within 6 hours. Only one of a group of 9 patients showed a relapse after a total dosage of 50,000 Oxford units and she responded to an additional amount of 100,000 Oxford units. A child aged 5 years with sulphonamide-resistant gonococcal vaginitis responded to a total dosage of 40,000 Oxford units. No toxic effects were observed in the series.

Safety of sulphathiazole treatment.—Among 904 female patients treated with sulphathiazole for chronic gonorrhoea, Strauss and Reibstein have encountered 3 cases of sulphathiazole poisoning. Positive cultures were obtained in all cases, positive smears in many. All these women were treated as in-patients and had routine laboratory tests including blood count, sedimentation rate and urinary examination before treatment was begun and at intervals during the course. Albuminuria, haematuria, anaemia and leucopenia were regarded as contra-indications. Minor toxic symptoms occurred in some other instances, but the following 3 patients showed more severe signs of poisoning. (1) A patient, aged 30 years, with gonorrhoea and congenital syphilis received 4 grammes of sulphathiazole daily for 5 days. Abdominal pain then developed, and after 2 days oliguria and haematuria. Ureteric catheterization did not show any obstruction and as on inquiry it was learned that the patient had attempted suicide by taking mercuric chloride 4 years previously, a diagnosis of nephrosis was made. The woman recovered. (2) A patient, aged 29 years, after receiving 4 grammes of sulphathiazole daily for 7 days became affected with jaundice, with positive direct Van der Bergh test. A history of pregnancy with eclampsia was elicited. Recovery took place. (3) A patient aged 21 years was given 4 grammes of sulphathiazole daily for 4 days and then there developed a number of apparently unrelated symptoms thought to be allergic in origin. The authors emphasize the safety of sulphathiazole provided that due care is exercised. Two of the above 3 cases of poisoning could have been avoided if more thoroughness had been observed in eliciting the history.

Of members of the Forces.—Speaking before the Medical Society for the Study of Venereal Diseases, Bolton described her experiences of in-patient treatment for gonorrhoea in members of the A.T.S. In a series of 250 cases, the patients were kept under observation for from 3 to 4 weeks. As re-infection is impossible, the reappearance of gonococci in the tests during this period is known to be due to a relapse. Adequate dosage is ensured; if the tablets are vomited they are crushed in milk and given as an emulsion, or intramuscular injections are substituted. The rate of cure by sulphonamides alone has been 94 per cent, in spite of the fact that many patients are antagonistic and ready to vomit their tablets. As soon as the diagnosis is confirmed the patient is put to bed and treatment by sulphonamides is begun. Local treatment is given only when trichomonas infestation is present (as it was in 25 per cent of this series), when there is a persistent cervical erosion or when complications occur. The routine dosage of sulphanilamide or sulphapyridine is 22.5 grammes spread over 6 days in diminishing doses and omitted at night. Of sulphathiazole 27.5 grammes is given in 5 days. Patients are encouraged to take plenty of fluid. Sulphathiazole rarely produces toxic symptoms. With sulphapyridine about 10 per cent of patients develop rashes. Vomiting occurs in a higher percentage. Anuria occurred in one patient who recovered. The results of treatment were as follows. Two hundred and twenty-six patients were given a single course of a sulphonamide with 90.4 per cent of cures. Of these 107 had local treatment for trichomonas infestation which unless treated from the start retards recovery from gonorrhoea. In the remaining patients, cure was obtained either by a second course of sulphonamide with fever therapy (5 cases), by intra-uterine glycerin applications (10 cases) or by a second course of a sulphonamide alone (9 cases).

Modern methods reviewed.—Osmond² describes a technique for the clinical investigation of the vulva, vagina and urethra in order to establish a diagnosis of gonorrhoea in the female. In acute cases the gonococci are easily demonstrable but in chronic cases examination, the best time for which is immediately after a menstrual period, may have to be carried out on 3 separate occasions before diagnosis can be made. The majority of acute conditions are cured by giving 1 gramme of sulphathiazole 4 times a day for 5 days in conjunction with sodium bicarbonate and a fluid intake of 6 pints daily. This routine can be repeated after an interval of 7 days if necessary; chronic cases, being resistant, often do need a repetition. Pregnancy does not contra-indicate such treatment. Local treatment in the form of dry or moist antiseptic swabbing once a day followed by an insufflation of powdered acetarsol or sulphanilamide is usually necessary only in chronic cases. Cervical erosions should be treated by topical applications of a substance such as mercurochrome. Complications, if resistant to chemotherapy, should be referred to a specialist. Tests similar to those used for diagnostic purposes should always be made once or twice at intervals of 4 days after treatment has been stopped and should be repeated at monthly intervals on 6 occasions before the patient can be pronounced to be cured. In addition, a gonococcal complement fixation test is useful in chronic cases. Vulvovaginitis is due generally to a cause other than the gonococcus but in cases which occur in a community of young girls, in which infection may spread rapidly, the patients concerned should be isolated. In order to establish a diagnosis in children, similar tests to those used in adult cases and modified when necessary, should be made. Except for purposes of general hygiene, local treatment should be avoided. Sulphathiazole in doses from

one-quarter to one-half of a tablet 3 times a day in early life rising to one tablet 3 times a day at the age of 5 years usually gives good results.

Gonorrhoea in both sexes

Diagnosis

Newer methods of diagnosis and treatment.—Speaking at the annual meeting of the Massachusetts Medical Society, Vose discussed recent advances in the management of gonorrhoea as they affect the general practitioner. The increased incidence which has accompanied the war has created a problem of military importance, and it is necessary for all doctors to make themselves conversant with the newer methods of diagnosis and treatment. With regard to diagnosis, increased reliance is now placed on culture to supplement the smear. During the last few years cultural methods have been developed to the point at which the results are considerably more accurate than are those given by smears; positive cultures are now obtained in many cases in which smears are negative. In private practice it may not be possible to use cultural methods and reliance must be placed on the results of clinical examination and of smears. As proof of cure, however, 3 negative cultures at weekly intervals are essential. Chronic discharge in which gonococci cannot be demonstrated is usually due to urethral stricture or prostatitis-vesiculitis in the male, to cervicitis in the female. These conditions must be treated before clinical cure can be obtained. Even in acute cases which respond well to chemotherapy, it is well to pass a bulbous bougie after clinical and laboratory signs of gonorrhoea have subsided in order to ensure that a stricture is not present. In the chronic cases assessment of cure may be very difficult and patients must be kept under observation for several months. Serological tests are of limited value and provocative measures are unreliable and may be dangerous. Chemotherapy is successful in curing well over 90 per cent of cases of gonorrhoea and has immensely reduced the incidence of complications. Sulphathiazole is the drug of choice. Fever therapy can cure refractory cases, but it is risky. Penicillin has great promise.

Dangers of the carrier

A warning about post-war epidemic.—Pelouze believes that an epidemic of gonorrhoea is imminent. He attributes the possibility to the easy acceptance by both medical and lay opinion of a belief based on insufficient evidence that the sulphonamide drugs effect complete cure in at least 80 per cent of cases within 5 days. Many persons regarded as cured are asymptomatic carriers. War conditions have increased promiscuous sex relationships and thus facilitate the spread of gonorrhoea. The development of sulphonamide-resistant strains through inefficient chemotherapy must be taken into consideration. Many physicians now question the accuracy of the former high rates of cure, and they doubt the correctness of the assumption that gonorrhoea in negro troops, as compared with white, responds better to sulphathiazole. The value of sulphathiazole as a prophylactic agent requires reassessment in view of the development of the disease after an interval of 2-4 weeks in persons taking the drug before and after exposure. Confusion of an asymptomatic carrier state with cure has led to statistical inaccuracy. The author cites an investigation which established by cultural methods a 32 per cent positive gonococcal carrier rate in patients rendered symptom free by one course of sulphathiazole. Further observation of these carriers revealed that in one month 47 per cent had become free from gonococci; that 34 per cent more were negative after the lapse of another month; that an additional 14 per cent yielded negative cultures at the end of the third month; that in 5 per cent, gonococci still continued to be isolated. A similar investigation in a large naval hospital in the United States of America revealed the gonococcus in 23 per cent of cases. Pelouze bases his forecast that a greatly increased incidence of this disease will occur on the commonness of the carrier state and on the length of time it may continue. A combination of chemotherapy and local treatment is required in at least 50 per cent of male cases in which cure can be controlled by cultural methods. In places in which this form of control is not available the combined treatment should be carried out in all cases.

Treatment

Penicillin by intravenous drip method.—Cook, Pool and Herrell have already reported favourably on the use of penicillin in cases of gonorrhoeal infection which show resistance to sulphonamide therapy, and now describe their observations on a further series of 14 similar cases in which equally good results were obtained by treatment with penicillin. Three of the patients were women with extensive pelvic involvement and in all cases blood cultures were positive for gonorrhoea. The penicillin was administered by the intravenous drip method which has proved very satisfactory in practice. Half the daily dose of penicillin was given in physiological saline solution morning and evening; the dosage ranged from 65,000 to 162,000 Oxford units and the duration of treatment was generally 2 or 3 days. The symptoms usually began to disappear a few hours after treatment was started. Dysuria was relieved within 4 or 5 hours. Negative blood cultures were obtained from each of the 11 male patients within from 14 to 48 hours. Two of the 3 female patients showed an equally satisfactory response but the third required 6 days' treatment because after 3 days it was found that the penicillin being used had lost its potency. During a second course of treatment with potent penicillin the blood cultures became negative and the symptoms subsided. In a few of the male patients it was noted that the urethral discharge persisted for a short time although cultures were negative. The discharge was probably caused by some secondary infection or it may have

been due to irritation from earlier local treatment. The ease of administration of penicillin and the small amounts required will probably lead to the general adoption of penicillin therapy in such cases. The patient experiences very little discomfort and no untoward reactions have been observed.

Report on 926 cases.—Bacteriological freedom during 3 months after cessation of symptoms should be the acceptable criterion of cure in gonorrhoea. After observing 926 cases Koch, Mathis and Geiger consider a lesser period to be inadequate and a longer period to be an unattainable ideal. The patients, seen at a municipal clinic, comprised 504 acute and 70 chronic cases in the male and in the female 222 acute and 130 chronic cases. Cases of less than 3 months' standing were classified as acute and cases exceeding 3 months as chronic. In males diagnosis was based on bacteriological findings in spread or culture or both of the urethral discharge or, if that failed, of the prostatic fluid. In females urethral and cervical spreads or cultures were employed. The first 98 patients each received approximately 32 grammes of sulphaniilamide in a fortnight. Eight patients were treated with sulphadiazine and 3 with sulphapyridine. Thereafter sulphathiazole was preferred, in two schemes of dosage. Half the number of the 817 patients received 1 gramme of sulphathiazole 4 times on the first day and then 0.5 gramme 4 times daily up to a total of 20 grammes in 9 days. The other half received 20 grammes equally divided over 5 days. Persistent discharge was combated with urethral instillations of silver solutions. Intravesical irrigations of potassium permanganate, employed at first in refractory cases, gave place to fever therapy. Vaccines were occasionally employed in chronic gonorrhoea. Patients who reported repeated attacks were not less responsive to treatment than were those with a first infection. To establish cure 3 consecutive negative cultures at weekly intervals during the 3 months after cessation of symptoms were required. Usually the passage of a sound, or other provocative test, was employed. Of the total of 926 patients, 286 were transferred; 640 remain for analysis and of these, 435 fulfilled the specified conditions. The remaining 205 although symptom free yielded positive cultures intermittently during the 3 months but after 3 months 10 only gave positive cultures.

The Chicago plan.—Bundesen, Bauer and Kendell make a preliminary report on the work of the Chicago Intensive Treatment Centre for venereal diseases. In dealing with gonorrhoea two routine methods of treatment are used, as follows. (1) Chemotherapy in the form of sulphathiazole which is administered to male patients in doses of 1 gramme every 4 hours, day and night, until a total of 18 grammes has been taken. Female patients receive 1 gramme 4 times a day, at 4-hourly intervals, until a total of 20 grammes has been taken. (2) Artificial fever is used in combination with sulphonamides for patients who prove resistant to chemotherapy. A patient is classified as sulphonamide-resistant if positive cultures for gonococci are still obtained after 2 routine courses of sulphonamide therapy. Before pyrexial treatment is given exhaustive clinical, X-ray, electrocardiographical and laboratory examinations are made. The treatment consists of a course of 7 grammes of the sulphonamide given over a period of 18 hours, immediately followed by 8 hours' maintained fever at 106° F. rectal temperature. The total number of patients included in the present report is 1,786, of whom 537 were males and 1,249 females. All entered the hospital voluntarily for treatment and only a very small number failed to complete the prescribed course. Of this total 106 were treated with artificial pyrexia plus a sulphonamide. The criterion of cure for male patients is one negative culture after disappearance of all clinical signs of gonorrhoea. In the case of female patients 4 consecutive negative cultures are demanded. All patients are under observation in the out-patient department for 3 months after discharge. The technique employed and the results obtained are to be the subjects of a subsequent report. The authors draw attention to the important preventive work being done at the Chicago centre, especially in connexion with the tracing of contacts.

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GOUT

See also B.E.M.P., Vol. VI, p. 37; Interim Supplement, No. 14*; and Cumulative Supplement, Key No. 579.

Aetiology*Historical review*

Biochemistry in modern research.—Neuwirth gives a historical account of gout through the ages. Its clinical manifestations were described by Hippocrates in the fifth century B.C. The Greek word for the disease was *podagra*, a trap, because it grips the patient's foot as a trap grips the foot of an animal. The English word is derived from the Latin *gutta*, a drop. Colchicum, under the name, hermodactyl, was used in the treatment of gout as early as the twelfth century and is still the chief drug used in relieving symptoms today. Sydenham (1624–1689) distinguished gout from other forms of arthritis and rheumatism and described the typical attack. Daniel Sennert (1572–1637) believed that the cause of gout was a morbid humour within the blood vessels. Scheele, a Swedish chemist, demonstrated uric acid in urinary calculi in 1776 and Wollaston found lithic or uric acid in gouty tophi in 1797. Garrod in 1848 reported that the blood of gouty persons contained abnormal quantities of uric acid in the form of sodium urate and considered that gout resulted from renal insufficiency. Since Garrod's day the biochemistry of gout has been extensively investigated, mainly with negative results. Modern research shows that an elevated level of blood urates occurs in many other conditions besides gout and many patients with tophaceous gout have normal blood urate concentrations. The cause of hyperuricaemia in gouty subjects remains unexplained. Colchicum, which alleviates the pain of gouty arthritis, has not any action on the urates in the blood or urine and the newer drug, cinchophen, which lowers the level of blood urate and increases the urinary output of urate is less certain in its action and more toxic than is colchicum. Some physicians now regard gout as an allergic reaction to an allergen derived from food, drink, bacteria or trauma. Tophi, the sole pathological proof of gout, first described by Galen, are found in only 50 per cent of all cases. Gout therefore still remains what Sennert called it in the sixteenth century, *opprobrium medicorum*, the physicians' shame.

Neuwirth, E. (1943) *Arch. intern. Med.*, **72**, 377.

HAEMOGLOBINURIA

See also B.E.M.P., Vol. VI, p. 115; and Cumulative Supplement, Key Nos. 588–593.

Clinical picture*Paroxysmal haemoglobinurias*

Exercise haemoglobinuria.—Palmer and Mitchell add 2 cases of march haemoglobinuria—one providing 3 months' observation—to 43 cases collected by Gilligan and Blumgart. The attacks consist in a rise in free plasma haemoglobin (haemoglobinaemia) and partial urinary excretion of the free haemoglobin (haemoglobinuria). They occur in the male only, between the ages of 16 and 35 years and persist usually for less than 2 years, without affecting general health. Upright exertion is essential to the occurrence of the attacks and attempts at reproduction by exertion while the patient is recumbent, stooping or cycling have failed. The patient minutely investigated was entirely normal except that he had a palpable spleen. His total plasma volume was assessed at 3,000 cubic centimetres and its haemoglobin content averaged 4.5 milligrams per 100 cubic centimetres at rest. After exertion this rose to a maximum of 40.3 milligrams, haemoglobinuria ensuing whenever 20.5 per cent was exceeded. The haemoglobinuria ended always within 3 hours of cessation of exertion and the maximum amount excreted at one paroxysm was equivalent to 7.9 cubic centimetres of whole blood. In all individuals senile erythrocytes continuously undergo destruction, liberating haemoglobin, some of which enters the plasma. Exaggeration of this haemolysis during erect exertion has been postulated to explain the haemoglobinuria. The absence of haemolysins in blood or urine, the lack of increase in faecal pigment and other evidence given confutes this theory. Saturation with ascorbic acid disproved that the administration of vitamin C had any effect; when the urine was rendered alkaline there was also not any effect on the paroxysms. Application of a tight abdominal binder and constriction of the limbs neither aggravated nor ameliorated the attacks and theories of venous compression as the cause were thus unsupported. It is concluded that some factor unknown interferes during erect exertion with the normal absorption by the reticulo-endothelial system of haemoglobin liberated by the destruction of senile erythrocytes and causes an overflow of haemoglobin into the urinary system.

Palmer, R. A., and Mitchell, H. S. (1943) *Canad. med. Ass. J.*, **49**, 465.

HAEMORRHAGIC DISEASES

See also B.E.M.P., Vol. VI, p. 138; and Cumulative Supplement, Key Nos. 596–603.

Primary non-hereditary haemorrhagic diathesis*The purpura*

Analysis of 500 cases.—Davis has analysed 500 cases of purpura seen by him during a period of 50 months, with the object of determining the incidence of the various types. The degree of purpura in the patients concerned varied from a few petechiae to the involvement

of the greater part of the skin. Benign cases were in a majority, severe cases rare. The ages of the patients ranged from a few hours to 89 years. Females were in a great majority in the rheumatic, familial and purpura simplex groups. The author has found no reason to believe that the incidence of purpura has increased as the result of the war, a fact which tells against the theory that purpura is caused by deficiency of vitamin P, if it is true that citrus fruits are the source of this vitamin. Of the present group of cases symptomatic purpuras formed 63 per cent. The aetiological factors believed to be of major importance in these 317 cases of symptomatic purpura were classifiable as follows: physical agents 7; chemical agents (gold, sulphapyridine) 5; bacterial disease 41; virus disease (measles) 1; spirochaetal disease 9; parasitic disease (trichiniasis) 2; cachexia 32; scnility 67; scurvy 5; metabolic and endocrine disorders 17; dermatological affections 7; alimentary disturbances 3; cardiovascular diseases 49; chronic nephritis 7; rheumatism 46; blood diseases 18; neoplasm 1. The association of purpura with rheumatism is noticeably common, especially in women and may have an endocrine basis. In many of the cases several of the above-named factors were at work. The remaining 183 patients were affected as follows: purpura simplex 78; Schönlein's and Henoch's purpura 14; hereditary familial purpura 79; haemorrhagic diathesis or pseudo-haemophilia, familial and non-familial, 7; thrombocytopenic purpura 4; haemophilia 1. The possibility of an allergic or rheumatic origin of some of these cases was considered. Of the 78 patients with purpura simplex 8 gave a history of urticaria, 15 of rheumatic fever; of the 79 patients with hereditary familial purpura 23 had had rheumatic fever. To classify this entire group as anaphylactoid is in the author's view unwarrantable.

Davis, E. (1943) *Lancet*, 2, 160.

HEADACHE

See also B.E.M.P., Vol. VI, p. 199.

Types of headache

Headache arising from the nose or sinuses

Investigation of symptoms and signs.—The vast majority of headaches are not of nasal origin, but Tremble points out that in headache of unexplained origin it is important to investigate the nose and the sinuses. Any obstruction of the nasofrontal duct, whether continuous or intermittent, is sufficient to cause headache. The vacuum headache is the result of absorption of the air in the frontal sinus after obstruction, and at times a little clear fluid, which shows only a few lymphocytes but not any polymorphonuclear cells, is also found. In cases of sinusitis, the throbbing nature of the pain, the situation and the time of the day when the headache occurs are of value in establishing a diagnosis. Pain over the frontal region and in the face or between the eyes is most often due to infection in the anterior group of cells (the frontal sinus, antrum or anterior ethmoidal cells) whereas pain over the vertex, behind the eyes and in the occipital region is more likely to be due to infection in the posterior group (the posterior ethmoid cells or sphenoidal sinus). The intermittent nature of sinusitis headache is dependent upon drainage; during the night the sinuses fill up with purulent material but with the adoption of the upright position drainage is facilitated. A chronic hyperplastic thickening of the mucous membrane of a sinus, due to an old suppurative process which has apparently healed or from an allergic response, does not lead to headache. Headache is not an early symptom in benign or in malignant tumours of the nose or sinuses; when it does occur it means that the growth is producing obstruction or suppuration. Whether sphenopalatine neuralgia is due to an inflammation in or around the ganglion or to an infection in the sphenoidal sinus is still a moot question. An important point in the differential diagnosis of nasociliary and anterior ethmoidal neuralgia—in the latter of which the pain is localized to the small area bounded by the supraciliary ridge above, the supra-orbital notch laterally and the nasal bones below—is that in true nasociliary neuralgia the application of cocaine to the nasal mucous membrane at the exit of the nasociliary nerve produces relief of pain. Vacuum headache is increased by movements of the eyes and pressure under the under part of the eyebrow. Suppurative disease is usually evident on X-ray examination. Pain due to sphenopalatine neuralgia disappears when cocaine is applied to the area behind the posterior tip of the middle nasal concha.

Tremble, G. E. (1944) *Canad. med. Ass. J.*, 50, 43.

HEART DISEASES: EXAMINATION

Examination for the Forces

Cardiologists and reclassification

Levy, Stroud and White report on the results of the re-examination by cardiologists of 4,994 men disqualified by local boards in the United States of America for military service on account of cardiovascular defects. The main problems presented were the significance of cardiac murmurs, the critical levels of blood pressure and heart rate, and neurocirculatory asthenia ('soldier's heart'). The number of men with cardiac and circulatory disorders amounted to 10 per cent of all those rejected for military service. The majority of the disqualified men were between 20 and 30 years of age; in this age group rheumatic heart disease was the commonest disorder, and there was also a higher incidence of neurocirculatory

asthenia than in other decades. The standards of physical examination and the criteria for rejection were those laid down in the mobilization regulations; many borderline cases were encountered. Electrocardiographical and radiological examinations were made when required. Of the whole group of 4,994 men originally rejected, 863 were subsequently reclassified as 1A and 4,131 were confirmed as 4F. The commonest cause among all age groups for final rejection was rheumatic heart disease, which was found in 50 per cent. Hypertension occurred in 21 per cent of the whole and neurocirculatory asthenia in 4.0 per cent. Sinus tachycardia, congenital heart disease, cardiac enlargement, arrhythmia, electrocardiographical abnormalities, cardiovascular syphilis, thyrotoxicosis, recent rheumatic fever, cardiac strain from chest deformities, coronary heart disease, pericarditis and peripheral vascular defects were responsible for rejection in the remaining cases. A high rejection rate was observed among negroes, Chinese and Filipinos. Hypertension and cardiovascular syphilis were more common among the negroes than among white men whereas neurocirculatory asthenia was much less common.

Levy, R. L., Stroud, W. D., and White, P. D. (1943) *J. Amer. med. Ass.*, **123**, 937.

— (1943) *ibid.*, **123**, 1029.

HEART DISEASES: CONGENITAL DISEASES

See also B.E.M.P., Vol. VI, p. 206; and Cumulative Supplement, Key Nos. 619–635.

Patent ductus arteriosus

Association with bacterial endarteritis

Transpleural ligation.—Harrington records a case from the Division of Surgery at the Mayo Clinic, of ligation performed through a postero-lateral approach of a patent ductus arteriosus associated with subacute bacterial endarteritis. In 95 per cent of cases seen at necropsy Christie found that the ductus arteriosus had closed in the first 12 weeks of life. The ductus arteriosus is peculiar to the arteriovascular system of the foetus. In cases in which the ductus arteriosus remains patent after birth there is a reversal of the blood flow; in the foetus the venous blood enters the aorta but after birth the arterial blood of the aorta flows into the venous blood of the pulmonary artery. Of the 6 patients in whom the author has ligatured the patent ductus arteriosus 2 had congestive heart disease, 3 showed minor episodes suggesting impending cardiac insufficiency and one, a girl aged 15 years, had the complication of bacterial endarteritis referred to above.

Pericardium

Absence of pericardium

Ronka and Tessmer describe a case of congenital absence of the pericardium. The condition was recognized when a young soldier with a perforating gunshot wound of the chest was operated on. At operation it was seen that the heart was free of any pericardial covering and was contained in the same serous cavity as the left lung. The patient died and at necropsy it was found that the anterior surface of the parietal pericardium was absent. There was a portion of the membrane over the ascending aorta anteriorly, for a distance of 3 centimetres vertically downwards, from a normal point of attachment at the beginning of the transverse part of the arch. The medial part of this pericardial membrane showed a continuous edge which circled beneath the lower part of the base of the heart and continued as a free edge of a second part of the pericardium at the left inferior side of the base of the heart. Between this point and the lower edge of the left auricular appendage the membrane appeared to fuse with the visceral pericardium along the atrioventricular groove. The heart weighed 350 grammes. The epicardium over the entire anterior surface was faintly grey and opaque. The great vessels and mediastinal structures were in normal relation. The function usually assigned to the pericardium is that of a restraining influence against overdistention of the heart, but Beck could find no evidence to support this view; Watt concluded that congenital absence of the pericardium is compatible with a long active life free from any special weakness of the heart. A separate pericardium is not essential for the normal working of the heart. A secondary function of the pericardium is to provide a nearly frictionless serous sac in order to aid the movement of the heart. The pleural cavity can take over this function.

Harrington, S. W. (1943) *Proc. Mayo Clin.*, **18**, 217.

Ronka, E. K. F., and Tessmer, C. F. (1944) *Amer. J. Path.*, **20**, 137.

HEART DISEASES: ENDOCARDITIS, MALIGNANT

See also B.E.M.P., Vol. VI, p. 297; and Cumulative Supplement, Key Nos. 644–646.

Subacute bacterial endocarditis

Treatment

Assessment of current methods.—Lichtman makes an attempt to assess the value of current methods of treatment of subacute bacterial endocarditis from his own series of 98 cases and from 606 cases collected from other sources. Cases inadequately treated or due to the gonococcus are not included. The author presents his review under 4 headings. (1) Reported cases of spontaneous recovery; of 2,596 cases recorded in the literature 1 per cent showed recovery. (2) Cases treated with sulphonamide drugs in which the recovery rate was 4 per cent of a total

of 489 cases. (3) Cases in which a combined form of treatment was used; Lichtman distinguishes 2 subdivisions here—(a) cases treated with sulphonamides combined with heparin and (b) cases treated with sulphonamides combined with artificial pyrexia. The former showed a recovery rate of 6.5 per cent. The methods of fever therapy used were of 2 types. Artificial hyperthermia yielded a 6.5 per cent recovery in 61 cases, while intravenous typhoid vaccine gave a recovery rate of 15.5 per cent in 45 cases. (4) Cases in which miscellaneous forms of therapy were employed; among these were radiotherapy with and without sulphonamides, injections of neoarsphenamine and surgical ligation of the ductus arteriosus in cases of subacute combined bacterial endocarditis superimposed on patent ductus arteriosus. The last-mentioned procedure has resulted in recovery in well over 50 per cent of patients but it is obviously applicable only to a small number of cases. Heparin is not without danger and persistent bacteraemia precludes its use. The author concludes that the results of current methods of treatment are disappointing although a small but significant number of patients recover.

Lichtman, S. S. (1943) *Ann. intern. Med.*, **19**, 787.

HEART DISEASES: MITRAL VALVE DISEASES

See also B.E.M.P., Vol. VI, p. 309; Interim Supplement, No. 16*; and Cumulative Supplement, Key Nos. 647–651.

Mitral stenosis

Clinical picture

Peripheral embolism resulting from digitalis therapy.—Massey and Steiner suggest the giving of digitalis as a possible cause of peripheral embolism. A young woman who was admitted to hospital with stomatitis received treatment with neoarsphenamine given intravenously, ascorbic acid given orally and 10 per cent chromic acid and potassium chlorate applied to the gums and used as a mouth wash. Concomitantly, mitral stenosis and auricular fibrillation required the administration of digoxin, totalling 5.25 milligrams, and 8 grains of digitalis folium given over 7 days. Bradycardia and vomiting caused pretermission on the seventh day. On that morning a cerebral embolus paralysed the left side of the face and left arm and in the evening the left leg became pulseless below the popliteal space. Embolectomy under local anaesthesia was performed at the level of origin of the profunda femoris artery. The femoral artery below the embolus remained contracted and later gangrene developed and amputation had to be performed. Again, in a second patient, a woman aged 28, mitral stenosis and auricular fibrillation were treated by the administration of digoxin, of which 2.5 milligrams were taken with evidence of therapeutic effect but not of overdosage, during 3 days. On the third evening signs of embolism appeared in the right leg, the popliteal artery being pulseless although the femoral artery pulsed with the thrusting impulse described by Heanley. An embolus situated as in the first case was removed and arterial spasm below the embolus was again observed. When the tunica adventitia around and for 1½ inches above and below the embolus was stripped pulsation returned and for 5 days remained exaggerated. Recovery ensued. Neither patient had previously taken digitalis, to which embolism was a sequel so immediate as to suggest cause and effect. The authors advocate embolectomy combined with Leriche's local sympathectomy for the simple and effective removal of the mechanical obstruction and for the nullification of the reflex spasm from the damaged endothelium.

Diagnosis

Early diagnosis of mitral disease

Use of fluoroscopy in children.—The early radiological recognition of mitral valve disease is discussed by Epstein. Mitral valve disease can be diagnosed with facility when the history and physical and X-ray evidence all indicate impaired valvular and myocardial function. Often however there is difficulty in making a positive diagnosis in children with an equivocal history and indefinite or transitory physical and X-ray findings. Demonstration of cardiac enlargement as soon as possible is important for diagnostic purposes. The earliest enlargement of the heart in mitral valve disease is left auricular enlargement. In order to find which radiological procedure is of most use in the diagnosis of early mitral valve lesions, the author examined 25 selected children by fluoroscopy in the right anterior oblique direction after administering a barium bolus. Even a small degree of posterior deviation of the oesophagus is significant and may occur a long time before the cardiac outline is otherwise changed. Other methods of determining cardiac enlargement, based on calculations made from telero-diagrams and the heights and weights of patients, were not found to be satisfactory in the demonstration of early left auricular enlargement. The frontal silhouette of the heart may appear to be normal even when the left auricle is enlarged posteriorly. It is necessary to appreciate these facts when examining patients with apical systolic or transitory murmurs. A murmur should not be diagnosed as functional if there is radiological evidence of enlargement of the left auricle, neither should a heart be judged to be normal if the murmurs are transitory or are temporarily absent and the left auricle is enlarged. Other criteria for determining enlargement of the left auricle include elevation of the left main bronchus, widening of the angle of bifurcation of the trachea, narrowing of the left main bronchus and the appearance of the left atrial border on the right cardiac edge. None of these changes was seen in the author's series of patients.

Treatment

General

Indications for use of various drugs.—Page reviews the indications for drug treatment in heart disease. The groups of compounds most commonly employed include (1) digitalis and its substitutes, and quinidine, (2) diuretics, (3) vasodilators and (4) opiates. The use of digitalis is now restricted chiefly to cases of congestive heart failure, regardless of aetiology. Although its value is most apparent in auricular fibrillation, especially that of rheumatic origin, favourable results have also been obtained in hypertensive heart failure with normal rate and rhythm. The drug should not be given indiscriminately for mere breathlessness or for cyanosis, nor is it immediately necessary in auricular fibrillation, especially in old people in whom subjective findings are absent. In cardiac dyspnoea without other systemic signs of heart failure, relief is often obtained by digitalis administration. In the early stages of coronary thrombosis it may be harmful, but if congestive failure occurs later its use may be indicated. It is probably not wise to omit the drug in cases of diminished cardiac reserve in which previously symptoms have been present. Strophanthus in the form of ouabain produces a more rapid effect and is useful in serious cases. Its early action can be subsequently supplemented by digitalis. Uginin, a mixture of the glycosides A and B of squill, may be used when intolerance of digitalis is present. Quinidine gives the best results in cases of auricular fibrillation of less than one month's duration and in auricular fibrillation due to hyperthyroidism. It is also useful in paroxysmal auricular tachycardia and has been used in coronary thrombosis. Theophylline derivatives and theobromine compounds are useful in congestive heart failure. Aminophylline (theophylline with ethylenediamine) is used as a respiratory stimulant and in cardiac asthma. The mercurial compounds, especially in conjunction with theophylline, are useful in heart failure which has not responded to digitalis and rest. Coramine (nikethamide) often has a beneficial effect in cardiac dyspnoea. Morphine may also be useful for the purpose of allaying restlessness and reducing blood pressure. Papaverine is beneficial in acute cor pulmonale with pulmonary embolism and in coronary thrombosis in the aged.

Diuretics

Mercurial diuretics and mercurialism.—McIntyre reports on the case of a woman with cardiac failure who was treated with mercurial diuretics for a long time. The patient, aged 55 years, suffered from essential hypertension with insidious cardiac failure. Her condition improved with reduction of weight, with rest and iodides and on a salt-free diet. Two years later auricular fibrillation developed and massive digitalis administration was instituted. The pulse had been maintained at a rate between 65 and 85. Five years after the onset of symptoms of cardiac failure cardiac dropsy intervened and, although it was recurrent for nearly a year during which time the patient was treated with salyrgan (mersalyl) and ammonium chloride, doses of 2 cubic centimetres of salyrgan given weekly have kept her practically free from oedema. In all, 680 injections have now been given. The only toxic symptoms have been a 'soapy' feeling in the mouth and 3 slight attacks of catarrhal colitis. The author concludes that there is slight risk of mercurialism after prolonged administration of mercurial diuretics provided that elimination is not impaired by renal disease and that oral sepsis is not present. Thrombosis is unlikely to occur if the patient's blood vessels are fairly healthy. Cramps may be prevented by an adequate salt intake and by the avoidance of dehydration.

Epstein, B. S. (1943) *J. Pediatr.*, **23**, 381.

McIntyre, C. M. (1943) *Brit. med. J.*, **2**, 609.

Massey, L. W. C., and Steiner, P. (1944) *Lancet*, **1**, 245.

Page, S. U. (1943) *Canad. med. Ass.*, **49**, 195.

HEART DISEASES: RIGHT SIDE DISEASES

See also B.E.M.P., Vol. VI, p. 357; and Cumulative Supplement, Key Nos. 653–658.

Hypertrophy

Diagnosis

Cor pulmonale.—Manning and Tillisch record a case, in an Italian male aged 23 years, of pulmonary hypertension and describe the evolution of the condition. The essentials now demanded in diagnosis are as follows. (1) Radiographical evidence of undue prominence of the pulmonary artery and right ventricle; (2) right axis deviation of the QRS complex in the electrocardiogram; (3) severe dyspnoea and cyanosis; (4) polycythaemia. Pulmonary arteriosclerosis was recognized in 1803 by Brisson but was regarded as being very rare until 1850 when Dietrich pointed out its common occurrence in mitral stenosis. From 1900 to 1935 secondary cor pulmonale was attributed to disease of the left side of the heart or to lesions of the parenchyma of the lungs and primary cor pulmonale to lesions of the pulmonary vascular bed. Since Brenner published in 1935 the results of his work on primary pulmonary hypertension, the disease has been regarded as one in which at necropsy a specific lesion cannot be found which would explain the clinical findings or the presence of a hypertrophied right ventricle. Secondary pulmonary hypertension may be due to mitral stenosis, emphysema, pulmonary fibrosis and other obstructive changes in the lungs. The clinical picture of pulmonary hypertension is not clear cut; the presenting complaint is often dyspnoea although it may not be severe. Cyanosis may or may not be associated with clubbing of the fingers.

Manning, J. J., and Tillisch, J. H. (1943) *Proc. Mayo Clin.*, **18**, 275.

HEART DISEASES: HEART FAILURE

See also B.E.M.P., Vol. VI, p. 368; and Cumulative Supplement, Key No: 659.

Clinical types*Congestive heart failure*

Radiology in investigating the causes.—Sosman emphasizes the importance of ascertaining the aetiological factor in cardiac failure. There are several groups of cases in which if the cause be recognized and removed, cure will follow. He refers to the help of the radiologist in this sphere and discusses 6 types of cardiac failure, 3 of which are amenable to surgical intervention and the others to medical measures. Hyperthyroidism, chronic constrictive pericarditis and patent ductus arteriosus comprise the surgical group. The condition of the heart may mask the underlying thyrotoxicosis. Clinical features which may give a lead in diagnosis are (1) undue loss of weight in spite of good appetite, (2) diarrhoea, (3) transient auricular fibrillation, (4) excessive perspiration and (5) periodic glycosuria. The alertness of the patient is often noticeably disproportionate to that which might be expected from the degree of heart failure. The vigorous, hyperactive and snappy beat seen in the X-ray examination is an important sign. The opposite condition of myxoedema results in marked hypo-activity of the heart beat as visualized in the radiological examination. Patent ductus arteriosus is a condition in which the majority of subjects succumb to cardiac failure or to subacute bacterial endocarditis. The findings by radiography are those of (1) left ventricular enlargement, (2) prominence of the pulmonary conus, (3) enlargement of the pulmonary vessels which also may show pulsation and (4) noticeable hyperactivity of the left ventricle with increased expansile pulsation of the pulmonary vessels synchronizing with ventricular systole. In the author's cases nearly all showed dilatation of the left auricle. Operation, involving ligation of the patent ductus arteriosus has proved to be successful in a large number of instances, and is best performed before the age of 15 and after the age of 4 years. Constrictive pericarditis, in contrast to the two preceding conditions, produces a diminution or absence of pulsations under X-ray examination. The heart may not be enlarged and is usually triangular in shape showing a blurring or absence of the normal curves. In normal hearts it is possible to recognize the auricular and ventricular junction by the difference in time of the respective beats of these chambers, but this distinction may not be possible in chronic constrictive pericarditis. Plaques of calcification were seen in many of the author's cases of chronic adhesive pericarditis but they may be absent, and furthermore calcification is not proof of constriction. The essential finding is that of right ventricular failure with a small or slightly enlarged quiet heart. Pericardectomy has proved most valuable in treatment of constrictive pericarditis. The first example of Sosman's medical group is cardiac disease secondary to vitamin B deficiency. Radiologically the features are those of a hyperactive heart beat and cardiac enlargement with return to a normal configuration after the exhibition of massive thiamine hydrochloride therapy. Nephritis and anaemia are recognized causes of cardiac disease and again their recognition may lead, with adequate therapy, to a satisfactory response which can be demonstrated radiologically. A rare malady is gummatous myocarditis which, unlike syphilitic aortic disease, offers very good hope of recovery with the administration of anti-specific drugs. The diagnosis from ventricular aneurysm and tumour must be considered.

Treatment by mercurial diuretics.—Modell describes studies designed to determine the relative effectiveness of different doses of mercurial diuretics. Only patients with chronic congestive cardiac failure in need of a diuretic were investigated. Each patient served as his own control by a comparison of the effects of alternate injections of different doses. In the period between injections oedema was allowed to return to its former level. Weight loss was used as a measure of diuresis. All subjects were ambulatory clinic patients, for only on them is it feasible to make a sufficient number of comparisons. Only one mercurial diuretic, mercupurin, was used. Patients were weighed immediately before their injections on one evening and again the following morning. The results show that the mercurial diuretics within the therapeutic range are relatively more effective as the dose of the drug becomes smaller. Very small doses however (0.5 cubic centimetre) produce too small an absolute diuresis to be of practical value. The effectiveness of a 1 cubic centimetre dose of mercupurin is about 60 per cent greater than that of a 2 cubic centimetres dose (per cubic centimetre) whether or not ammonium chloride or other supplementary drugs are used. The total effect of the repeated 2 cubic centimetres doses for the entire series was only 20 per cent greater than for the 1 cubic centimetre doses. The use of ammonium chloride increases the diuretic action of either dose by about 15 per cent in the average case. Benefits may be obtained by giving a patient two 1 cubic centimetre injections instead of one 2 cubic centimetres injection a week. These benefits include not only the 20 per cent greater total diuresis but greater comfort and less danger to the patient. The effect of intramuscular and intravenous injections of the same dose of mercupurin is about the same. The use of intramuscular injection often causes moderate local tenderness but it eliminates serious immediate reactions.

Heart failure in old age

Factors in prognosis.—Howell reports on the nature of heart failure in the aged from a series of 75 male patients whose ages ranged from 62 to 92 years. He emphasizes the differences existing between old age and earlier life in the aetiology and clinical features of cardiac failure. Hypertension was present in 33 cases, coronary disease in 17, myocardial toxæmia

in 11; the remaining 14 comprised various cases including 10 of uncertain origin. Left ventricular failure occurred in 16 cases, right heart failure in 13, a combination of right and left failure in 9, coronary thrombosis in 10, angina pectoris in 4 and progressive cerebral ischaemia in 15 (in 3 associated with right heart failure); cardiac stoppage was encountered in 3 instances and other forward failure in 5. The common occurrence of multiple aetiology is stressed. Arteriosclerosis plays a part both by producing external resistance to the output and by lessening the nutrition of the myocardium. The final impression of the author is that the level of the blood pressure and the state of the arteries are the two deciding factors in prognosis.

Howell, T. H. (1944) *Brit. Heart J.*, **6**, 20.

Modell, W. (1944) *Ann. intern. Med.*, **20**, 265.

Sosman, M. C. (1943) *Radiology*, **41**, 351.

HEART DISEASES: GENERAL

Treatment

Glycosides

Cedilanid.—The cardiologist's ideal drug is one which is effective, standardized and non-toxic. Parsonnet and Bernstein commend lanatoside C, a glycoside isolated from *digitalis lanata*; the preparation actually used was cedilanid. Hitherto standardization has been unsatisfactory. The frog method of assessment is misleading. The cat method neglects the varying absorbent powers of different intestinal tracts. As cedilanid is crystalline it is standardized by weight. Experiment showed that cedilanid excelled all other glycosides of *digitalis lanata* in safety in use and in the production of cardiac efficiency and that it did not reduce significantly the coronary blood flow. It was stable and daily administration for 3 months was not deleterious to dog's heart muscle. Clinically Fahr and LaDue obtained satisfactory results in auricular fibrillation, in paroxysmal tachycardia and auricular flutter and in congestive heart failure even in the presence of normal rhythm. Present observations concern 100 patients of whom 25 had never taken digitalis. The average oral dose necessary to bring the patient under the influence of digitalis was from 7.5 milligrams to 10 milligrams of cedilanid. The average maintenance dose was from 0.5 milligram to 1.5 milligrams. The disappearance of oedema, of ascites and of hepatic enlargement, the lowering of pulse rate and of venous pressure and electrocardiographic records served as criteria of improvement. Action and elimination proved to be rapid. A maintenance dose, once established, could be continued. Two patients with auricular fibrillation failed to respond to cedilanid although both responded to whole leaf digitalis. Probably such cases require combined glycosides or some glycoside other than cedilanid. The notable advantages of cedilanid are consistency of action, wide margin of safety and rapidity of elimination.

Parsonnet, A. E., and Bernstein, A. (1943) *Amer. Heart J.*, **26**, 39.

HEMIATROPHY AND HEMIHYPERTROPHY

See also B.E.M.P., Vol. VI, p. 416; and Cumulative Supplement, Key Nos. 662–664.

Acquired hemiatrophy

Partial hemiatrophy

Localized lesions of cerebral cortex.—Penfield and Robertson describe cases which show that limitation of growth of part of the body may be produced not only by a lesion of the spinal cord occurring in early life or by a large injury of the opposite hemisphere of the brain, but also by exactly localized lesions of the cerebral cortex alone which occur in infancy. Many authorities have written on growth asymmetry and many explanations have been given of its occurrence but there does not appear to have been any previous attempt at a correlation of growth asymmetry and the presence of cerebral scars. The 32 cases presented were those of patients with epileptic attacks due to local cerebral lesions, operated on at the Montreal Neurological Institute and the Royal Victoria Hospital, Montreal, during the 10 years between 1928 and 1938. Local anaesthesia was used, the position of the rolandic cortex was defined by electrical illumination whenever possible and the relation of the lesion to this area was established. The cases fell into 3 categories, namely (1) those in which there was bodily asymmetry, (2) those in which a lesion dating from childhood occurred in the cerebral rolandic cortex and (3) those in which there were definite areas of asymmetry anywhere in the cerebral hemisphere, provided the lesion dated from childhood. Study of the cases with bodily asymmetry showed that the factor common to all was involvement of the post-central cortex, either alone or with the internal capsule or with the internal capsule and the pre-central cortex as well, this last group producing the most pronounced asymmetry. The conclusions drawn were that infantile lesions of the post-central gyrus limit the growth of the contralateral part of the body—the arm and leg almost invariably, the thorax and face usually—whereas lesions of the frontal occipital and temporal portions of the cerebral cortex do not produce growth changes. Decrease in the length and size of the bones with moderate muscular atrophy is caused by injury to the post-central gyrus which occurred before the age of 2 years; there is no final evidence that after this age similar lesions would not inhibit growth. A large lesion of the central region of the hemisphere causes a greater degree of diffuse somatic atrophy than

does a lesion of the post-central gyrus alone. This greater degree of atrophy may be due to disuse or to involvement of subcortical structures but there is no evidence to show which. Contralateral hypertrophy of the body is not produced by lesions of the cortex, nor is there any evidence that such lesions cause vasomotor changes in man.

Penfield, W., and Robertson, J. S. M. (1943) *Arch. Neurol. Psychiat., Chicago*, **50**, 405.

HEREDITY AND CONSTITUTION

See also B.E.M.P., Vol. VI, p. 452.

Dominant, recessive, and sex-linked inheritance in man

Sex-linked inheritance

Unusual occurrence of imbecility.—Martin and Bell describe a family in which a history of imbecility in 11 males of two generations was obtained. The mothers concerned were mentally normal, and all but one were the daughters of two brothers; the one excepted was their sister. The two brothers were said to have been normal and the hypothesis put forward is that some controlling factor caused suppression of the disease in them without affecting their liability to transmit it. In spite of certain difficulties the authors believe that the mental defect is due to a sex-linked recessive gene. In two known instances relatively slight mental deficiency was observed in females of the family and in these, it is suggested, the causal gene was incompletely recessive. It is rare to find such a hereditary history in mental deficiency and the authors refer to certain cases which have been elsewhere described as 'sex-linked microphthalmia sometimes associated with mental deficiency'; in this latter family group there was not any mental deficiency except in association with blindness. There was no evidence that Martin and Bell's cases were progressive; in this way the disease differs from other hereditary cerebral diseases and it is suggested that it was due to an error of development.

Constitution

The concept of organic unity

Psyche and soma.—In an interesting article Draper treats of the concept of organic unity in relation to psychosomatic medicine. The duality of man—what might be called a tangible phase, the body or soma, and an invisible phase, the psyche—has always embarrassed physicians, and the relation between the two aspects has been and still is a point of controversy. In the term, psychosomatic medicine, it was attempted to combine the two parts, but the term still seemed to express a dichotomy—two parts which work reciprocally on each other—rather than a biological unity. From the beginning of this century many observers have attempted to examine the organism as a whole; here their example is Aristotle, who considered the living creature as greater than its parts and endeavoured to find an order and unity in each living thing. A second concept was that the material basis of life is not one protoplasm but many, the differing qualities of which are inherent in the cells. A third concept concerns the circulating fluid elements of the body and the reciprocal effects of neighbouring cells and tissues. Other observers have shown that the cell, taken as a specialized centre of action, is nevertheless made to modify its speciality in order to serve the needs of the organism when necessity arises. Turning to the imponderable invisible phase, Draper considers the term, psyche, in relation to disease to be the quality which distinguishes a living organism from a dead one, to be therefore the life force manifested through protoplasmic response to stimuli from without or within. He gives the case histories of 2 patients with multiple ailments, in order to illustrate the underlying organismal unity. In one all the symptoms were somatic, but an emotional stimulus was postulated as an additional factor. In the second there was a known emotional factor. When this unity was realized, understanding of the patient followed and cure was possible. Shock therapy is one of the newer advances in organismal treatment and also supports what the author calls the 'biological concept of living protoplasm in continuity, subserving an integrated and vital whole'.

Draper, G. (1944) *J. Amer. med. Ass.*, **124**, 767.

Martin, J. P., and Bell, Julia (1943) *J. Neurol. Psychiat.*, **6**, 154.

HERPES

See also B.E.M.P., Vol. VI, p. 513; Interim Supplement, No. 11*; and Cumulative Supplement, Key Nos. 688 and 689.

Herpes zoster

Clinical picture

Associated motor disturbances.—Motor disturbance is rare in herpes zoster and Taterka and O'Sullivan could collect records of 42 cases only, Broadbent's description in 1866 being the first. The authors add 2 cases. Cases involving the cranial nerves are excluded. Analysis of the 44 cases shows that the proportion of males to females afflicted is nearly 3 to 1. In 20 patients the upper extremity was involved, the trunk muscles in 18 and the lower extremity in 6. The eruption precedes the paralysis in 75 per cent of cases; in the remainder the paralysis precedes the eruption. In either event the interval varies from one day to 2 months. The eruption and paralysis affect always the same side and usually the same segmental distribution. In 81·2 per cent of cases there was a reaction of degeneration or diminished response. The first case

described concerns a man aged 60 years whose right quadriceps femoris muscle was affected and the second a woman whose right deltoid muscle was atrophied and paralysed. The treatment of both consisted in a high vitamin diet; 10 milligrams of thiamine hydrochloride 3 times a day were given orally, as well as ultra-violet rays and galvanism, and exercises were prescribed. Both patients recovered almost completely in a year although Brain states that such palsies are usually permanent. The analysis shows a recovery rate of 16 per cent. In case (1) the patient displayed fibrillary twitches indicating involvement of the anterior horn cells. Fibrillation was not reported in any other patient and its absence has been emphasized. Despite a history of injury in case (1) the relation of herpes zoster to injury remains indeterminate.

Ramsay Hunt syndrome.—The association of the typical cutaneous eruption of herpes zoster with a disease of the peripheral nerves was established by von Bärensprung in 1861. A year later, in a case in which autopsy was performed, he described the inflammatory changes in a dorsal root ganglion and related portion of the spinal nerve. In the region of the cranial nerves 2 special syndromes are common, 'ophthalmic herpes' and 'geniculate herpes'. The combination of paralysis of the facial nerve and auricular herpes, with or without deafness, tinnitus and vertigo was first ascribed to a herpetic lesion of the geniculate ganglion by Ramsay Hunt (the Ramsay Hunt syndrome). Hunt however described post-mortem changes in only one case, a case in which the geniculate ganglion was not examined. Denny-Brown, Adams and Fitzgerald have now described the clinical features and post-mortem changes in 3 cases of the disease. Their virus studies on rabbits proved to be negative but they carried out a very detailed microscopical and histological examination in each case. The histological investigation revealed (1) a ganglionitis with necrosis of all or part of the ganglion, sometimes with haemorrhage, surrounded by intense lymphocytic infiltration and associated with the characteristic eruption; (2) a unilateral poliomyelitis with segmental localization; (3) a relatively mild leptomeningitis limited to the involved spinal segments and nerve roots; (4) a true peripheral mononeuritis in the nerves distal to the ganglion and also in the anterior nerve root, both within the meninges and in the portion contiguous to the involved spinal ganglion. These changes account for the neuralgic pains, the persistent pleocytosis and the local palsies. In one of the authors' cases, which showed the Ramsay Hunt syndrome, the geniculate ganglion was entirely unaffected. There was a typical necrotizing ganglionitis (second cervical ganglion) and motor neuritis of the facial nerve. The authors conclude that evidence for geniculate ganglionitis in the Ramsay Hunt syndrome is invalid and that it is possible that some of the various herpes zoster syndromes with palsy of the facial nerve depend upon the concurrent involvement of two or more cranial nerves.

Herpes simplex

Clinical picture

Immunity tests.—Berry and Slavin have carried out experiments on herpetic infection in mice. An inbred strain was used. Spontaneous encephalomyelitis had never been encountered in the colony. Female mice, about 6 weeks old, were immunized by means of graded doses of unattenuated HF strain of herpes simplex virus, of which the sixty-sixth to ninety-third mouse brain passages were used. About half the number of mice so treated died of herpetic encephalomyelitis. The survivors were then mated and their offspring were tested for immunity at the age of 2 weeks by inoculating them intranasally with a 10 per cent suspension of infected mouse brain. For each litter born of an immune mother one born of a non-immunized mother was inoculated at the same time, as a control. Of 115 of the former, 94.8 survived; out of 101 of the latter only 2.9 per cent survived. Antibodies were demonstrated by neutralization tests in the blood of the young mice born of immunized mothers. The route of transmission was shown to be the milk by removing certain litters from their mothers and allowing them to be suckled by foster mothers. Mice suckled by non-immunes showed a survival rate of only 8 per cent whereas mice born of non-immune mothers and suckled by immunes showed a survival rate of 100 per cent. By further experiments upon other litters at a later date resistance was shown to have diminished considerably by the end of the fifth week of life, that is the third week after removal from the mother. Young mice could be given an equal degree of protection by subcutaneous and intradermal injections of immune rabbit serum. Herpes virus was not recovered from the foetuses of either immune or infected mothers, showing that the immunity developed in the young is of passive character.

Berry, G. P., and Slavin, H. B. (1943) *J. exp. Med.*, **78**, 305.

Denny-Brown, D., Adams, R. D., and Fitzgerald, P. J. (1944) *Arch. Neurol. Psychiat.*, Chicago, **41**, 216.

Taterka, J. H., and O'Sullivan, Mary E. (1943) *J. Amer. med. Ass.*, **122**, 737.

HISTOPLASMOSIS

See also B.E.M.P., Vol. VI, p. 520.

Morbid anatomy

Occurrence in a young child

To the 53 known cases of histoplasmosis Beamer, Smith and Barnett add that of an infant aged 11 months. In the literature 42 cases were spread throughout the United States of America and 11 cases were distributed between Panama, the Philippine Islands, South America,

Honduras, Java, England and South Africa. The causal organism was first described by Darling in 1906 as akin to the Leishman-Donovan body and was named by him *Histoplasma capsulatum*. In 1934 De Monbreun proved it to be a fungus of two phases, yeast-like in the tissues and mycelian in cultures. The authors' patient displayed a virulent septicaemia, respiratory difficulty and, from the fourth day of life, a generalized impetigo. The liver and spleen were enlarged and the blood showed 3,600,000 erythrocytes and 16,000 leucocytes per cubic millimetre. *Staphylococcus aureus* was cultivated from the throat and the blood. Death ensued on the eighth day of acute disease, 14 hours after admission to hospital. Necropsy showed enlargement of all thoracic and abdominal lymphatic glands. Yellow-gray foci, disseminated throughout lungs, liver, spleen, kidneys and large intestine, proved microscopically to consist of phagocytes engorged with the yeast-like form of *H. capsulatum*. Cardiac blood was utilized for smears and the inoculation of blood agar plates. Smears showed leucocytes which contained yeast-like forms, some of which were partially extruded. Extracellular forms were heavily encapsulated. The agar plates when incubated aerobically at room temperature displayed mycelian colonies on the fourth day. Incubation, aerobic and anaerobic, at 37° C. produced *S. aureus* only. In young mice which were inoculated with a suspension of pulped spleen histoplasmosis developed. Cultures persisted throughout incubation for several weeks at 80° C. although growth was inhibited. The infant's intestinal lesions suggested his diet of pasteurized milk to be a possible vehicle, but the organism in milk succumbed within 20 minutes at 63° C. Whether the path of invasion is alimentary, respiratory or cutaneous, or perhaps insect-borne, remains unsettled.

Beamer, P. R., Smith, E. B., and Barnett, H. L. (1944) *J. Pediat.*, **24**, 270.

HYDATID DISEASE

See also B.E.M.P., Vol. VI, p. 538; and Cumulative Supplement, Key Nos. 692–701.

Life-cycle

Man as a second host

Methods of infection.—Barnett depicts the life cycle of *Taenia echinococcus*, the parasite which spreads hydatid disease. This cestode in the tapeworm stage inhabits the small intestine of the canine tribe and the close association of man and dog is the predominant factor in human infection. The terminal oviparous segment or proglottis when ripe passes in the faeces which on desiccation are spread by wind and flies over pasture, vegetation and water. The ingested eggs lead to the hydatid stage in the second hosts—sheep, cattle and pigs. At their death the lungs, liver and other infected offal are often devoured by the canine tribe in which *T. echinococcus* again develops. Such is the general cycle, but man too may be the second host, in which case the ingestion of the eggs is effected by the dog's caresses and by eating raw vegetables. Hand to mouth infection is also common from contact with wool or with the cow's udder. The swallowed egg develops into the oncosphere in the small intestine, the wall of which it penetrates in order to reach the liver, lungs and more rarely other regions. In these viscera cysts are formed which have 2 walls containing fluid under pressure, the whole encircled by a fibrous capsule. From the inner wall (endocyst) are developed the scolices or embryonic heads of future tapeworms. Exceptionally the parent cyst converts some of the scolices into daughter cysts, undergoes gelatinous or calcareous degeneration, and suppurates or is expelled through respiratory, alimentary or urinary channels. Hydatid disease is endemic in South America, Australia, New Zealand and South Africa and along the Mediterranean seaboard and is sporadic in Great Britain. Preventive measures include the dosing of dogs with vermifuges, restraining dogs from feeding on raw offal and protecting food and water supplies. Such measures have hitherto failed from lack of legislative support.

Barnett, L. (1944) *Med. Pr.*, **211**, 8.

HYDROCEPHALUS

See also B.E.M.P., Vol. VI, p. 566.

Treatment

Congenital hydrocephalus

Good results with vitamins E and B complex.—Hitherto only occasional success has rewarded the treatment of congenital non-obstructive hydrocephalus. Stone reports good results in 9 cases, 5 with accompanying meningocele, which were treated by administration of the vitamin E of wheat-germ oil and the vitamin B complex. Four cubic centimetres of a mixture containing one part of the oil and 4 parts of vitamin B complex were administered thrice daily in feeds or by dropper to children over 2 years of age and half that amount to infants. This initial dose was adapted to the patient's progress by varying the amount of oil. The medication has continued with benefit for a period of up to 2 years. Improvement was general, notably in arrest of hydrocephalus, reduction of nystagmus, improvement of vision, increase in intelligence and development of muscular tone. The cessation of spinal fluid rhinorrhoea, complete healing of a broken-down meningomyelocele sac and absorption of subcutaneous exudate in the lower limbs were notable features in a patient displaying Fröhlich's syndrome. Three hydrocephalic patients with optic atrophy who originally showed little or no response to visual stimuli later reacted correctly for objects held before

them. Two patients with early hydrocephalus who were operated on for meningocele while receiving medication, healed well without development of hydrocephalus. Deficiency of vitamin E in the expectant mother may be the cause of hydrocephalus in the child; otherwise the relief of hydrocephalus may be due to the effect of vitamin E on capillary permeability. The effect of vitamin E on tissue exudates in arthritis deformans, fibromyositis, muscular dystrophies, cretinism and hydrocephalus suggests that the vitamin should be given a therapeutic trial in nephrosis, nutritional oedema and oedema of unknown origin.

Stone, S. (1943) *J. Pediat.*, **23**, 194.

HYDROTHERAPY

See also B.E.M.P., Vol. VI, p. 573; and Cumulative Supplement, Key Nos. 703–707.

External application (balneotherapy)

Baths

Review of various types.—Behrend reports on 10 years' experience of a modern hydrotherapy department during which time 75,000 cases were treated. He states that the immunizing function of the skin can readily be stimulated by full baths of increasing temperature, for example in measles and scarlet fever. The condition and appearance of the skin, its nutrition and age, are of greatest significance in the reactions which are caused by external stimulation. Many mild neuroses without apparent cause respond well to suitably selected mild hydrotherapeutic measures. During the course of bath treatments the so-called thermal reaction is often seen. Clinically this shows itself after the first week in general fatigue, increase of original pain and restlessness. With further treatment these symptoms subside. Sometimes a second reaction is seen after three weeks' treatment. The blood pressure may rise and sleeplessness and constipation ensue, with fever leucocytosis and increased blood sedimentation rate. It is essential to guide the patient successfully through the thermal reaction. Behrend emphasizes the value of partial baths of increasing temperature particularly in cases of peripheral vascular diseases. The steam jet has now been found to be indispensable; it causes an immediate dilatation of skin capillaries followed by a deep-reaching hyperaemia. Its great pain-relieving effect was seen in sciatica and in acute bursitis around the shoulder joints. Patients with chronic arthritis were treated in a tank of water in which a whirlpool effect had been contrived. The application of the galvanic current in a full bath is a useful form of therapy; the water produces a perfect contact over a large skin area for the transmission of the electric current. The duration of a single treatment varied from 15 to 45 minutes. An increase of symptoms may occur after from 2 to 4 treatments. After the bath the patient must rest for at least half an hour and preferably for one hour. Massage should be given when it is indicated. The conditions treated by Behrend were all of the rheumatic group. Best results were obtained when pain was the dominant symptom.

Behrend, H. J. (1944) *Arch. phys. Ther.*, **25**, 5.

HYGIENE AND PUBLIC HEALTH

Prevention of infection

Dust-laying oils

Application to hospital bedclothes.—Harwood, Powney and Edwards describe a new technique for the application of dust-laying oils to hospital bedclothes. In the course of preliminary small-scale tests on wool it was found possible to discharge on to fabrics almost the whole of the oil from a dilute oil-in-water emulsion stabilized with a certain concentration of cetyl pyridinium bromide, provided that the liquor was maintained in a slightly alkaline state, for example at a hydrogen ion concentration of 8. The British Launderers' Research Association undertook to oil all the bedclothes, hangings and so forth from certain scarlet fever and measles wards at the London County Council North-Western Hospital, after they had been washed and rinsed in the hospital laundry. During a period of 4 months 4 tons of articles were treated in ordinary washing machines. Two aqueous solutions of technical white oil were used, (1) a positively charged emulsion with fixanol C (cetyl pyridinium bromide) as the stabilizing agent and (2) a negatively charged emulsion stabilized with teepol (sodium salts of sulphated secondary alcohols). The first could be used for pure woollen articles, but cotton fabrics or a mixture of wool and cotton needed the negatively charged emulsion in order to obtain complete deposition of the oil. It is considered that, given the correct washing technique, the method can be employed on a large scale by any hospital laundry.

Report of hospital test.—Wright, Cruickshank and Gunn report on the results of a controlled test carried out in two measles wards of the London County Council North-Western Hospital in 1943 on the efficacy of oiled blankets, ward-linen, garments and floors in preventing the spread of dust-borne infection. Two similar wards were used for the test over a period of 12 consecutive weeks. Type VI haemolytic streptococcus, sulphonamide-resistant, was found to account for 90 per cent of all cross infections and of all middle-ear complications occurring after admission. In the control ward no measures were taken against dust-borne infection; in the test ward for the first 3 weeks the floor only was treated with spindle oil. This was found ineffective as a preventive. In the remaining 9 weeks the floor was re-oiled every 4 weeks and all bedclothes, garments, towels, curtains and so forth, were treated with technical white oil

during laundering. With this procedure the mean bacterial and haemolytic streptococcus counts in the air during sweeping and bed-making varied from 91 to 99 per cent less in the test ward, and in this ward the percentage of type VI cross infection was 18.6 compared with 73.3 in the control ward. The middle-ear complication rates in the two wards were respectively 2.8 and 14.3 per cent. The oiling technique effectively controlled air-borne streptococcal infection but did not prevent cross infection from direct contact or mediate means.

Application in military barracks.—Anderson, Buchanan and MacPartland describe an experiment arranged to test the value of oiled floors in diminishing the spread of air-borne infections among soldiers in barracks. The experiment was carried out between December 1942 and March 1943 and involved the men in two army units (of strength from 1,300 to 1,700), A and B, each of which was a training centre occupying one complete barracks. The floors of unit A were treated with spindle oil once a month; 1 gallon of oil was enough to treat about 1,000 square feet of floor space. In unit B, used as a control, the floors were untreated. In each unit the men lived and worked under almost identical conditions and in each set of records were included all cases arising *de novo* of recent upper respiratory catarrh with obvious local signs, and all cases of a generalized 'influenzal infection' accompanied by pyrexia. It was found that in unit A, with oiled floors, the average rate of respiratory infection was 7 per 1,000 men, compared with 38 per 1,000 in the control unit, in which there also occurred a serious outbreak of respiratory infection of almost epidemic proportions between the middle of February and the first week in March. In the test unit no such outbreak occurred during the whole period of the experiment.

Social medicine

Outlook for the future

Social medicine, according to Buzzard, embraces the whole of Medicine. The progress of its curative branch, appealing to the imagination of the public and of the profession, is assured. The Government is considering schemes for the improved treatment, without any financial liability, of all sick persons. Simultaneously attention is concentrated on preventive medicine lest institutions and practitioners be submerged by remedial responsibilities. Five deficiencies demand to be made good. Study has disclosed the immediate cause of many diseases but too often the remoter causes elude detection. Research is the first desideratum. Secondly, in the medical curriculum preventive medicine should enjoy equality with curative medicine. Thirdly, the instruction of the public in hygiene by authorities official and voluntary should be more successfully carried out. The cooperation of practitioners with district nurses and with almoners promises more fruitful results. For the fourth deficiency the State and Local Boards are responsible. Until bad housing and inadequate nutrition are remedied, capital invested in medical services cannot return a reasonable dividend. Fifthly, attractive conditions of livelihood are required in order that men and woman may be recruited to the medical profession. Coordination between practitioners and medical officers of local authorities would mean a saving of time for men already in harness. Institutes of social medicine can contribute research, instruction and integration. Research must be largely in the social field and the data provided by the practitioner would be elaborated by the bio-statistician of the Institute. Instruction, of which the technique is undetermined, would embrace the medical student and the public. Integration connotes the cooperation of practitioner, lay worker and scientific expert.

Anderson, P. H. R., Buchanan, J. A., and MacPartland, J. J. (1944) *Brit. med. J.*, 1, 616.

Buzzard, F. (1943) *Practitioner*, 151, 129.

Harwood, F. C., Powney, J., and Edwards, C. W. (1944) *Brit. med. J.*, 1, 615.

Wright, Joyce, Cruickshank, R., and Gunn, W. (1944) *Brit. med. J.*, 1, 611.

HYPOGLYCAEMIA AND HYPERINSULINISM

See also B.E.M.P., Vol. VII, p. 42; Interim Supplement, No. 13*; and Cumulative Supplement, Key No. 712.

Clinical picture and course

Stages

General review of hypoglycaemia.—Himwich reviews the physiology, pathology, symptoms and treatment of hypoglycaemia. It is important to maintain the level of blood sugar in the body because if it is reduced below the lower normal limits the brain is deprived of its food-stuff, glucose. Only one mechanism, the parasympathetic-insulin apparatus, acts to limit a rise in blood sugar, but several intricate mechanisms work against a fall in blood sugar. The latter factors are the sympathetic-adrenaline apparatus, the thyroid gland and posterior lobe of the pituitary gland, and also the anterior lobe of the pituitary gland and the adrenal cortex. Hypoglycaemia may arise from failure of the liver, from excessive insulin and from disturbance in the neuro-endocrine defences. When hypoglycaemia arises the symptoms are the same irrespective of the cause and fall into a sequence of 5 stages. This sequence is ascribed to different metabolic rates in the various regions of the brain, the highest rate being found in the newest portions developmentally. The areas with the most intense metabolism will be the first to suffer on withdrawal of energy. (1) In the first or cortical phase, symptoms are due to depression of cortical and cerebellar functions and include sweating, salivation, tremors and

clouding of consciousness. (2) In the second or subcortico-diencephalic phase there are formative movements like grasping and sucking, and other primitive and aimless movements like snarling and restlessness. (3) In the third mesencephalic phase tonic spasms, squints and extensor plantar responses occur. (4) During the fourth pre-myelencephalic phase recurrent short extensor spasms are seen. This stage gives warning of (5) the succeeding perilous myelencephalic phase in which parasympathetic signs predominate. Respiration is shallow, heart rate is slow, pupils are contracted, tendon jerks are diminished. This fifth stage is due to the release of the lower part of the medulla and its centres. If glucose is given at any time up to and including the first 15 minutes or so of the fifth phase, recovery occurs through the stages in reverse. Barbiturates diminish the motor activity of hypoglycaemia. The symptoms of hypoglycaemia in an infant are mild because its metabolism is much lower than that of the adult.

Himwich, H. E. (1944) *Amer. J. digest Dis.*, 11, 1.

ICHTHYOSIS

See also B.E.M.P., Vol. VII, p. 52.

Ichthyosis simplex

Vitamin A deficiency

Disturbance in vitamin A metabolism.—Experiment shows that disturbances in vitamin A metabolism may be reflected in the cutaneous changes which occur in keratosis follicularis and in pityriasis rubra. In the hope of finding a similar relation between vitamin A metabolism and skin conditions in ichthyosis Peck, Glick and Chargin investigated 2 cases of congenital ichthyosis. The first was that of a boy aged 15 years who had suffered from ichthyosis since birth. Studies of dark adaptation showed a cone threshold at the upper level of the normal, providing little evidence of vitamin A deficiency. The normal vitamin A blood content is between 60 and 100 United States Pharmacopeia units per 100 cubic centimetres of serum. Here, first examination in April showed 20 U.S.P. units of vitamin A and 29 micrograms of carotene per 100 cubic centimetres of serum. The patient received daily 200,000 units of vitamin A orally, which ultimately raised the blood content to 139 U.S.P. units of vitamin A and 79 micrograms of carotene per 100 cubic centimetres of serum. Improvement was striking but the tendency of ichthyosis to improve in summer was borne in mind. With December came recurrence, although the serum maintained a satisfactory vitamin A content. Substitution of intramuscular injections for oral administration failed to show improvement by use of the latter method; oral administration was resumed but deterioration continued. Resumption of intramuscular injections of vitamin A concentrates and of cod-liver oil was abandoned owing to local reactions. Summer's advent again brought amelioration although vitamin A was not administered. The second patient was a woman aged 36 years with ichthyosis from birth. The rod and cone threshold was well above the normal. The serum contained 34 U.S.P. units of vitamin A per 100 cubic centimetres and 15 micrograms of carotene. Again the vitamin A content was readily raised and improvement occurred during the summer. Again with October came relapse. Oral or intramuscular administration readily raises the serum content of vitamin A to the normal levels but its maintenance over long periods does not ameliorate the course of ichthyosis.

Peck, S. M., Glick, A. W., and Chargin, L. (1943) *Arch. Derm. Syph., N.Y.*, 48, 32.

IMMUNITY AND IMMUNIZATION

See also B.E.M.P., Vol. VII, p. 58; and Cumulative Supplement, Key Nos. 720-733.

Active immunity

Leucocytosis

Stimulating factor in exudates.—The existence of a factor which stimulates the production of leucocytosis and which occurs in various types of inflammatory exudates has already been demonstrated by Menkin. The same author has now studied the effect of the leucocytosis-promoting factor on the growth of cells in the bone marrow of dogs. The animals were killed 2 or 3 days after they had been given from 1 to 3 intravenous injections of a solution containing the factor, and the bone marrow changes were studied by microscopy. Bone marrow samples from 2 untreated dogs and from 2 control dogs which had been injected with the pseudo-globulin fraction of normal serum were also examined. An extreme hyperplastic reaction was observed in the bone marrow of the 2 dogs which had been injected with the leucocyte-promoting factor, with many myeloblasts, myelocytes, megakaryocytes and mitotic figures. In the other animals there was no apparent hyperplasia. The occurrence of acute leucocytosis may be determined by the activity of the bone marrow at the time when the factor is introduced into the circulation by injection. Thus with a relatively aplastic marrow there would be a comparatively slow response. It is possible that the maturation of leucocytes already circulating in the blood may also be accelerated by the same factor but this remains to be investigated in further studies which have been already started. The leucocytosis-promoting factor appears to be without any detectable or injurious action on other tissues of the body. Clinically the factor may be of importance in the treatment of agranulocytic and aplastic conditions of the bone marrow and in various infective diseases in which the prognosis

depends partly upon the leucocytic response. In its present state of purification the factor can induce a rise of from 70 to 400 per cent in the circulating leucocytes.

Menkin, V. (1943) *Amer. J. Path.*, **19**, 1021.

IMPOTENCE

See also B.E.M.P., Vol. VII, p. 103.

Treatment

Organotherapy

Testosterone propionate in cases of aspermia.—Huhner describes aspermia as a rare condition in which coitus attains neither orgasm nor ejaculation. Both are attainable by masturbation and occur in nocturnal emission, the semen containing vital spermatozoa. Azoospermia differs radically. Here ejaculation occurs but on account of obstructed genital tubes or endocrine abnormality spermatozoa are absent. Aspermia is of unknown causation and dates usually from puberty, although temporary aspermia may result from repeated ungratified stimulation. Organic disease of the nervous or reproductive structures has not been detected. Advice to undertake coitus under alcoholic influence in order to overcome a surmised psychic inhibition has proved unavailing. In the first case now considered a habit of masturbation with prostatic congestion was initially overcome. After 18 injections of testosterone propionate in the form of perandren, each of 25 milligrams, administered 3 times a week, coitus was twice normally completed. After further injections at 5-day intervals, but with the dosage increased to 50 milligrams, the patient reported normal conditions; one slight relapse 6 months later quickly yielded to resumed treatment. The second patient, aged 32 years, complained of partial impotence for some years and aspermia since undergoing bilateral sympathectomy for arterial hypertension. He received 550 milligrams of perandren in 9 injections, which produced matutinal erection, but dizziness and vomiting compelled cessation of treatment.

Huhner, M. (1944) *J. Urol.*, **51**, 178.

INDUSTRIAL MEDICINE

Fatigue and its causes

Effect of noise

Factors to be considered.—McCoy discusses the analysis and interpretation of industrial noise and their significance in preventive treatment. The noise level metre should be calibrated immediately before the inside inspection of the building; the metre should be held in the hands or rested on a quiet surface while readings are being taken. The noise level taken is that at the ears of the workers subjected to the noise, with the microphone at a 90° angle from the noise source. Noise level readings should also be taken in passages and at points in a noisy area where people must work, and records for individual job noise levels should be kept. The interpretation of the noise survey of noise dangerous to health should be made according to various factors: (1) the sound intensity, (2) the total time and periods of exposure, (3) the type of ear defender, including the constancy of its use, (4) the distinction concerning the type of noise—continuous or interrupted, (5) the immediate environment from an acoustic standpoint, (6) the technical possibility of its elimination, (7) the physical condition of exposed employees and (8) the frequency of the noise. Subjective tests of noise would not give quite comparable results because of processes of adaptation which may mask damage to the ears. The wearing of ear stoppers should be encouraged.

Injuries

Eye injuries

First aid in eye injuries.—Dickson¹, director of the Ross Foundation (Scotland), discusses the report of the Foundation on the new first-aid treatment of eye injuries in industry with 10 per cent albucid soluble (sodium sulphacetamide) eye drops as recommended for collieries by the Ministry of Fuel and Power. The treatment, involving 14,451 injuries, has been tested over a period of 18 months in 30 collieries and in 30 factories in Scotland. Between 95 and 99 per cent of the injured so treated returned to work without loss of working time and Dickson strongly recommends the adoption of the treatment in all kinds of industry. In all cases of eye injury the patient should report immediately to the ambulance room for treatment. For the removal of foreign bodies a small rubber sponge is to be preferred to a brush. Preventive measures mentioned are the use of a face screen of perforated zinc in coal mines where picks are used on coal liable to splinter, of glass shields to cover abrasive wheels and of protective goggles. The ship-building industry affords the greatest incidence of eye injury, no fewer than 44 per cent per annum of the employees being affected; welder's flash is the most common form of injury. In other industries the majority of eye injuries are caused by fragments of metal or abrasive matter.

Value of albucid.—Dickson² states that annually some 8,000 industrial ophthalmic injuries which cause over 3 days' disability, are compulsorily reported. If lesser injuries are included, the total approaches 250,000 according to his estimation. The miner and the metal worker at the lathe are peculiarly exposed. Immediate resort to the ambulance room is desirable, since neglect or amateur treatment may convert trivial injury into total blindness. Foreign bodies in the cornea, if superficial, are removed in the first-aid room, preferably by means of

a rubber sponge rather than a camel-hair brush. If fragments are embedded, the cases are referred to the medical officer. If they are below the surface, absence of pain for some hours may cause delay in seeking treatment. Radiographical localization of foreign bodies may be necessary and, if they are metallic, their removal by the use of a magnet. The pain of corneal abrasions leads to early and therefore successful treatment. Chemical burns respond slowly with liability to relapse after apparent cure. Prophylaxis requires the examination and correction of vision of workers on engagement, and periodical superintendence. The provision of protective appliances attached to machinery is the responsibility of the employer and sometimes ingenious devices cut off the light if their use is neglected. Goggles, individually fitted, visors of celluloid or perforated zinc and gauze veils are also supplied; the employee is responsible for their use. The infection of corneal wounds, which may lead to ulceration and hypopyon, arises from the existing conjunctival flora, especially the pneumococci, and in 23·8 per cent of cases blindness of the affected eye used formerly to ensue. The introduction of albucid soluble (sodium sulphacetamide) for first aid has improved the outlook greatly by preventing infection.

Dickson, R. M. (1943)¹ *Brit. J. Ophthalm.*, **27**, 544.

— (1944)² *Brit. J. phys. Med.*, *N.S.*, **7**, 77.

McCoy, D. A. (1944) *J. Industr. Hyg.*, **28**, 120.

INJURIES

See also Interim Supplement, No. 18*.

Wounds

Infections and complications

Effect of dicoumarin on post-traumatic gangrene.—Brambel and Loker investigated the administration of dicoumarin (dicoumarol) in trauma and gangrene. After trauma the coagulation property of the blood is enhanced; the authors observed a similar effect after internal or external haemorrhage. A period of 24–48 hours elapses before dicoumarin produces any change in the coagulability and its effects are often unpredictable. Heparin has no 'latent period' and was therefore used in some cases for an initial rapid effect. The clinical material consisted of a series of cases of post-traumatic gangrene after injury, diabetic and arterio-sclerotic gangrene and frost-bite. Injury to the endothelium of blood vessels, excessive liberation of thrombokinase, swelling of tissues and accelerated prothrombin clotting time all favour the development of thrombosis; dicoumarin antagonizes such tendencies. Ten cases of crush injury were treated successfully. Dicoumarin was administered orally as soon as the patient was able to swallow; heparin was given in some cases initially. Overdosage of dicoumarin was prevented by regular testing of the plasma prothrombin time. Three patients with diabetic gangrene and one with arteriosclerotic gangrene associated with marked uraemia were treated. In the last-mentioned case dicoumarin had to be discontinued after a single dose, because of the prolonged effect obtained on the prothrombin time; jaundice also developed, but it was considered that dicoumarin was not a contributory cause. This case record confirms the contra-indication of poor renal function to dicoumarin therapy. In the diabetic group sulphonamides were employed in conjunction with dicoumarin and no antagonistic or toxic actions were seen. The authors consider that the administration of dicoumarin was of much value in inhibiting the gangrenous process. One example of frost-bite gangrene of the feet was treated, and the extension of the destruction was checked. Hepatic damage was not witnessed in any of the cases, although dicoumarin was continued over a period of several months in one instance. The authors claim that when dicoumarin is administered the site of amputation can be more distally located. The total amount of dicoumarin given varied from 300 milligrams (a single dose) to 4,800 milligrams.

Head and face

Air in the cranial cavity.—Money and Stoller review the subject of air in the cranial cavity. Air may pass into the tissues of the scalp or enter the cranial cavity as a result of fracture or erosion of the cranial air sinuses. Extracranial pneumatocele is a relatively minor disorder and the air remains in the subaponeurotic layer of the scalp or tissues of the orbit. Injury to the anterior portion of the skull may be followed by cerebrospinal rhinorrhoea and at the same time allow the immediate passage of air into the cranial cavity. Extradural collection of air is an extremely unlikely occurrence, since the pressure of the entering air could hardly strip the dura mater from the skull unless this had already been done by arterial haemorrhage or at operation. The dura is thinner and more adherent over the bones of the paranasal sinuses than it is elsewhere, therefore dural tears and erosions are commoner in this site. If the air remains sterile it may be absorbed within a few days or even after months. If infection accompanies the entry meningitis will result, and if the air has made a pocket for itself in the substance of the brain infection may produce a brain abscess. Skull erosion secondary to chronic infective processes (particularly tuberculosis and syphilis) and to neoplasms is an avenue of entrance of air, while anaerobic infections may be mentioned as a rare cause. Extracerebral pneumocephalus may result as a breakdown of early repair tissue which produces at the same time secondary rhinorrhoea, the onset being some time after the injury; coughing, sneezing and other forms of straining may be the precipitating factor in such instances. The subdural space may be the site of the air and here the prognosis is good if the

brain and leptomeninges remain intact. In the subarachnoid space the air may pass into the ventricular system. The brain substance may contain the air and a fistulous track from the ruptured cortex to the subarachnoid space ensues, or if the opening on the brain surface heals a cyst-like cavity results. Air may enter the ventricles by means of rupture through their walls. A possible mode of spread is from the sphenoidal sinus directly through a distended third ventricle. The symptoms may be grouped as those due to (1) local trauma, (2) increased intracranial pressure (especially if the portal of entry is valvular) and (3) infection. The one infallible sign is the X-ray appearance. Treatment consists of rest, avoidance of all straining efforts and administration of sedatives if indicated. Sulphonamides should be administered prophylactically. If the pneumocephalus is not being absorbed or is increasing, operation is indicated to close the portal of entry of air. Methylene blue injected intrathecally colours the escaping cerebrospinal fluid and localizes the track. Should the opening be small the application of silver nitrate locally may suffice, but in most cases a major operation for repair of the defect will be necessary.

Main principles of treatment of face injuries.—A few simple rules for treating soft tissue injuries of the face are summarized as follows by Slaughter. (1) Arrest of bleeding should be carried out as far as possible by pressure; ligatures should be used sparingly and should be of non-absorbable material. (2) Prevention of additional trauma and contamination is provided for by a clean dressing. The only bactericidal agent used should be sulphanilamide powder, and this only if some hours must elapse before surgical cleansing is undertaken. (3) The patient's general condition must be considered and if necessary treated. (4) Surgical cleansing of the wound must be carried out under fully aseptic conditions. Soap and boiled water should be used and antiseptics avoided. If the wound is contaminated with grease and so on, the use of a grease solvent is necessary. All foreign bodies must be removed. If they are embedded in the skin a spud or similar instrument should be used to dig them out. Careful suturing of the wound without tension is essential in order to avoid unnecessary scarring. The deeper parts of the wound are brought together with buried interrupted sutures of fine silk or cotton and the skin edges with a continuous subcuticular stitch of nylon or horsehair. (5) Dressings are not used unless they aid in the fixation of the injured parts. If used they should be changed as seldom as possible. The rules given above are designed to provide good apposition, to avoid unsightly scars and to prevent permanent tattoo marks due to the presence of foreign bodies.

Wounds of the upper facial region.—Oldfield, opening a discussion on the early treatment of war wounds of the upper part of the face at a conference of medical officers in the Middle East, mentioned first the importance of immediately applying a firm dressing, in order not only to stop bleeding but also to hide the injured face from other soldiers. Morphine is then administered and the patient is taken to the casualty clearing station, lying on his side or prone on the stretcher if blood running back through the mouth or nose causes respiratory difficulty. At the casualty clearing station thorough cleansing with soap and water is followed by irrigation with peroxide and then with saline or acriflavine. Foreign bodies and detached fragments of bone are removed. A sulphonamide is then insufflated into the wound and a tulle gras and saline dressing is applied. If the wound has perforated into the mouth, with loss of tissue, skin is stitched to mucous membrane round the edges of the defect. If a facial wound is recent and without skin loss it may be sutured with fine silk stitches which are removed 2 or 3 days later; otherwise it must be left widely open. Wounds of the forehead involving the anterior wall of the frontal sinus are treated by cleansing the sinus and draining it into the nose through a small rubber tube surrounded by a Thiersch graft. If the posterior wall of the sinus is fractured and the dura torn the patient should be transferred to the care of a neurological surgeon.

Treatment of war wounds of the face.—Converse discusses in the light of his experience the treatment of war wounds of the face, fractures of the facial bones with cerebrospinal rhinorrhoea and comminuted fractures of the malar bone with ptosis of the eye-ball. If permanent discoloration of the scar is to be avoided wounds of the soft tissues must be cleansed from foreign material. Because of the remarkable resistance of the face to infection debridement can be sparing. Three principles must be observed: (1) avoidance of tension; (2) elimination of raw areas; (3) preservation of the anatomical position of remaining tissues. Whenever it is possible facial wounds should be sutured immediately. If this is not possible, during the waiting period the wound should be packed with sulphanilamide-Vaseline gauze. When loss of tissue is extensive immediate skin grafting is advisable. For burns sulphanilamide ointment is applied after cleansing. Deep burns are excised about the tenth day and a split graft is applied. The problem of fractures with cerebrospinal rhinorrhoea is difficult; if deformity is reduced intracranial damage may be increased; each case must be considered individually. Closure of the tear in the dura is usually advisable if this fails to take place spontaneously within a few days, because of the constant menace of meningitis. Stereoscopic X-ray examinations and laminographs are necessary in order to estimate the amount of bony damage. The presence of air in the ventricles is an absolute indication for operation. Comminuted fractures of the malar bone with ptosis of the eye-ball are serious if unreduced, because of the resulting permanent diplopia. After stereoscopic X-ray examination operation is carried out by a dual approach through the antrum and through the skin over the fracture. Replacement and wiring are carried out and the floor of the orbit may require the support of a pack or of a mould in the antrum; the latter is to be preferred.

Trunk

Penetrating chest wounds.—In a review of 291 cases of penetrating chest wounds treated by a surgical chest team in North Africa from April 1941 to May 1943, Nicholson and Scadding discuss methods of treatment and results obtained. In their opinion the best situation for a chest team is at a forward base hospital to which patients can be evacuated from the front line. In the authors' series surgery in forward areas was usually confined to closure of sucking wounds by suturing the deeper layers firmly and loosely stitching the skin over a soft paraffin pack. Visceral surgery in such an area is very limited in character and pulmonary foreign bodies were rarely removed. Shell, bomb and mine fragments were retained more frequently than were bullets, although many thoraco-abdominal wounds were due to bullet penetration. Sulphanilamide was given as a routine by mouth. Staphylococcal infections were prevalent. In haemothorax early aspiration is advisable as air replacement leaves the pleural cavity open to infection. The authors state that the danger of a recurrence of haemorrhage after aspiration has been exaggerated. In their cases infected haemothorax was drained or if necessary rib resection was performed. If a pleural foreign body is present it should be removed at this stage. Much tissue damage favours clotting with the occurrence of clotted haemothorax. In most of the 65 cases of pulmonary contusion the patients recovered. There were cerebral complications in a few cases. In thoraco-abdominal wounds in which diagnosis is difficult, the abdomen should be opened rather than the chest. The giving of a high protein diet with the addition of vitamin C is important. The giving of transfusions and the carrying out of respiratory exercises are necessary in simple and infected haemothoraces.

Injuries of the ureter.—McIver reviews injuries of the ureter and their management. Wounds of the ureter alone are rare. Of these 25 cases are surveyed; 14 were attributable to direct trauma and 11 to indirect trauma. Gunshot and stab wounds require immediate operation particularly when they involve the peritoneal cavity. Accidental injury of the ureter at the time of surgical operations if not recognized results in complications, the most common of which are fistula, peritonitis and renal infection. The average period for the development of fistula is 12 days; of the author's 9 cases, it complicated hysterectomy in 5 and removal of a large retroperitoneal ovarian cyst in 2; in the remaining 2 it was a complication of excision of the rectum and rectosigmoid. Manipulation of a ureteral calculus resulted in 6 instances of trauma; McIver emphasizes the necessity of using instruments with gentleness in all intra-ureteral manipulations. He also considers that cases of injury of the ureter should be treated surgically, promptly and with provision for adequate drainage; ureterostomy, pyelostomy and nephrostomy are employed in order to combat infection and obstruction. The ureter which is injured in the manipulation of a calculus should be catheterized immediately and the catheter left in place; if this is impossible operation may re-establish the lumen or failing this, re-implantation of the ureter into the bladder, bowel or skin should be attempted. Nephrectomy, however, may prove to be the only possible procedure.

Crush injuries*General*

The crush syndrome.—Bywaters reviews the subject of crush syndrome, in particular ischaemic muscle necrosis and impaired renal function. After the release of a person, part of whose body has been pinned under debris, the general condition may not at first cause any concern. The limb or area involved may show erythema of the skin and perhaps blister formation. Within a few hours, however, the part becomes swollen and hard and the affected muscle insensitive and paralysed. If the process progresses, diminution of the distal pulse, with pallor and coldness of the area, occurs. The underlying muscle is pale and necrotic, the marked increase of pressure is due to exudation of plasma and the artery is found to be in spasm. Histologically, changes in the muscles are found at necropsy. Associated with the local alterations, signs and symptoms of shock appear. Whereas in some patients the peripheral vasoconstriction may be able to combat the fall in blood pressure, the continued loss of plasma may overcome this compensatory mechanism. Plasma transfusions at this stage will produce relief. Acid haematin is contained in the first specimens of urine and later numerous coloured casts of myohaemoglobin are found; the amount of urine passed progressively decreases until at the end of the first week as little as 25-50 cubic centimetres in 24 hours is voided. About one-third of the number of patients recover. On the sixth or seventh day a critical diuresis occurs. The potassium of the blood increases in the terminal course of the affection owing to a diffusion of muscle potassium and impairment of potassium excretion from renal failure. Post-mortem examination shows the kidneys to be swollen and tense with necrosis of the distal convoluted tubules. The essential lesion of crush injury is muscle necrosis. The exact pathogenesis of the disorder requires further elucidation. Non-milky fluids and alkali are essential and should be given orally in first aid—if possible before release. These measures should be continued until the urine is alkaline; if vomiting occurs intravenous administration should be performed. Serum or plasma should be given for the shock before the blood pressure falls and morphine for the pain. For local treatment ice-bags should be applied. Fascia-splitting incisions may be required if circulatory obstruction occurs. Further cooperative work between physician, surgeon and pathologist is needed in order to establish the effects of therapy, especially in cases with renal failure.

Head and face

Treatment of the smashed-in face.—The value of tracheotomy or laryngotomy in the first-aid

treatment of the smashed-in face is emphasized by Patey and Riches. The essentials of treatment are control of bleeding and primary approximation of the soft tissues and fractured bones. Treatment must be carried out under anaesthesia and the administration of an anaesthetic is rendered incomparably easier and safer if a preliminary tracheotomy or laryngotomy is performed under local anaesthesia. Moreover in many cases of severe facial smash injury respiratory embarrassment is caused by blood running into the pharynx, and this in its turn tends to increase the amount of bleeding. Under general anaesthesia asphyxia may supervene. Once a clear airway is established emergency treatment can readily be carried out pending the transfer of the patient to a special unit. When bleeding has been controlled and gross damage to bones and soft tissues dealt with the eyes should be inspected, with the help of small retractors inserted under the swollen lids, and an ophthalmologist's aid obtained if necessary. A careful watch should be kept for evidence of cerebrospinal rhinorrhoea which necessitates neurosurgical help. The administration of one of the sulphonamides may be of assistance in preventing local sepsis and aspiration pneumonia.

Blast injuries

Trunk

Clinical effects of immersion blast.—Webster, Ross and Alford, summarizing recent reports of blast injuries to the abdomen, included reports by Wakeley, Gordon-Taylor, McMullin, Auster and Willard and their own observations on 15 survivors of a torpedoed ship. The men sustained abdominal injuries from an exploding depth charge while they were swimming in the water around the vessel, which sank in about 4 minutes. The survivors all gave a fairly uniform history of having received a tremendous blow on the abdomen, 4 men stating that they were paralysed or knocked unconscious for a short time. Soon after being rescued they all had severe abdominal pain and vomiting. The degree of shock varied considerably; some men with extensive injuries were able to walk ashore 12 hours after the explosion. When they were admitted to hospital all were suffering from severe abdominal pain; some had cramp, but in most cases the pain was of a stabbing character. All vomited repeatedly, several with blood and bile and 9 had bloody diarrhoea. All were feverish, with a temperature averaging 102° F. Five became distended and almost all developed abdominal rigidity. Four patients died, one on the first day, one on the second day, one on the fifth day and one 6 weeks later; 4 had protracted periods of convalescence; 7 recovered rapidly and were discharged from hospital in from 3 to 14 days. From these and other cases the following features are emphasized, (1) the tremendous force of the blast and (2) the almost complete absence of respiratory symptoms. The mortality among those brought ashore alive was 21.4 per cent. Webster, Ross and Alford recommend that sailors be warned of this danger in the event of disaster at sea and be advised to swim as quickly as possible away from the sinking ship, to keep turned away from it and when opportunity presents to pull themselves as far as possible out of the water; that life-preservers be made of kapok and designed to cover the abdomen and chest; that treatment of shock and blood loss be instituted early and include transfusion of blood and plasma; that medical practitioners in coastal areas should appreciate the urgency of early treatment, both medical and surgical, and be encouraged to report cases at once; that Naval base hospitals should be prepared either to send surgical and transfusion equipment to the scene of action by airplane or to transport patients promptly to a place where treatment is available; that early chemotherapy be seriously considered; that in doubtful cases the patient should have the benefit of laparotomy.

General

Course and prognosis

Significant effects of water-soluble derivatives of chlorophyll.—Smith and Livingston investigated the efficacy of topical application of various medicinal preparations in relation to the healing of experimentally induced wounds and burns. The results were controlled by comparison with a series of similar lesions which were allowed to heal naturally. The authors were particularly interested in the possible value of chlorophyll, and solutions, jellies and ointments of this substance were included in the tests. Chlorophyll (water-soluble) appears to possess the property of stimulating fibroblastic growth in tissue culture and has also bacteriostatic properties. The mode of action is obscure. The results of the experiments showed that chlorophyll exerted a significant effect in accelerating the healing of both traumatic and thermal wounds. An important further observation made was that of the comparative ineffectiveness of any of the vitamins applied locally. While much of the recent work has emphasized the value of an adequate vitamin C intake in wound healing, its local action as judged from the authors' studies is negligible. Compounds of the sulphonamide group actually caused retardation of the healing process except in the presence of active infection when the resultant delay in healing is more than offset by their value in controlling infection. Methionine was employed for the purpose of supplying the growth-stimulating sulphhydryl radical; no clear conclusions could be drawn from the small numbers tested. Scharlach R was inert and tetrodine had properties similar to those of the sulphonamides. On the basis of their observations Smith and Livingston suggest that chlorophyll preparations should be used more extensively in the treatment of wounds and burns.

Treatment

Essentials in skin grafting.—The importance of early application of skin to any raw surface is emphasized by McIndoe. Slow healing spells deep fibrosis, contractures and deformities.

Skin loss may result from trauma or from burns. The chief difference, from the practical standpoint, between the two types is that in burning an initial period of sloughing must elapse before a clean base is obtained whereas with early excision of wounds a clean base is left immediately. A plaster case is excellent for the growth of granulations and repair of bone but it does not encourage the growth of skin. In compound injuries plaster cases should always be removed as soon as possible and skin loss, now clearly defined, should be made good by grafting. Primary grafting may be carried out within the first 24 hours in wounds of the face but not after such a long interval elsewhere. For delayed grafting a healthy granulating surface must be secured. The best method of preparation is by saline and half-strength eusol pressure dressings applied over tulle gras. Specific antiseptics may be necessary. The state of the healing edge and its rate of spread are more reliable than organism counts as the basis of a decision whether or not a surface is suitable for grafting. Five varieties of grafts are available: (1) small deep grafts spaced not more than 1 centimetre apart over the raw surface; (2) 'postage stamp' grafts of split skin arranged patchwork fashion on tulle gras with gaps of $\frac{1}{2}$ inch between and applied thus to the raw surface; (3) epidermal grafts, chiefly of use for eyelids; (4) split skin grafts, which are applied on tulle gras under pressure and which should be perforated by multiple stab holes to allow drainage; (5) pedicled flaps, used chiefly for gunshot wounds of the hands and feet, compound fractures of the legs and loss of skin around the heel.

Modern methods of skin grafting.—In a Discussion on modern methods of skin grafting Mowlem stated that for a successful free skin graft the area must be recently prepared, uninfected and vascular and that the graft should be kept in close apposition to the area for from 2 to 10 days. The split skin graft is used for immediate repair of wounds and for covering extensive skin losses. Whole thickness grafts are used for cosmetic reasons, for example on the face and in areas where freedom from secondary contracture is essential. The grafts are fixed to the area by suture of the margins to the recipient area, and by applying a filled mould of paraffin-flavine cotton-wool. The mould is then tied on and pressure is applied to the area by elastoplast or crepe bandage. There are three ways of transplanting skin: (1) by free skin grafts, (2) by local flaps and (3) by flaps from a distance (Jayes). Robb-Smith described a study made by Converse and himself for the healing of donor areas. A thin graft ($\frac{1}{1000}$ inch) was removed. This included the whole of the epidermis and some of the superficial dermis, but not the sebaceous glands and hair follicle roots. Two days later a biopsy from the donor area showed blood clot and fibrin. On the third day the epithelium was beginning to grow out. On the thirty-second day the donor area showed a normal epidermis including regeneration of the elastic fibres which are so necessary for flexible skin. When a thick graft of $\frac{5}{1000}$ inch was removed, there was only slight epithelization by the fifth day which was not complete until about the sixty-fifth day, with no formation of elastic fibres. Gabarro used chess-board grafts for skin grafting. These are grafts of suitable thickness cut into squares with $\frac{1}{4}$ -inch or smaller sides. A graft of this size permits free draining. Dressing of a wound by the method is rapid; Gabarro was able to graft and dress 200 squares in less than one hour. They 'take' in different types of raw areas where other grafts have failed. The small square is also useful in plastic surgery and in war surgery as it will take on areas which are in bad condition and will give good results.

Skin grafting by coagulum contact.—Sano describes her coagulum contact method of skin grafting and reports the results obtained in 10 cases. The method of preparing the medium is as follows, the whole process being carried out under sterile conditions. Five cubic centimetres of the subject's blood are drawn into a 10 cubic centimetre syringe containing 1 milligram of heparin dissolved in 1 cubic centimetre of Tyrode's buffered salt solution. The mixture is centrifuged and the plasma is placed in a 5 cubic centimetre test-tube. To the residue left after centrifuging, or to the leucocyte layer alone, 1.3 cubic centimetres of Tyrode's solution are added and the mixture is shaken with glass beads to ensure thorough disintegration of the cells. If the erythrocytes have been included the mixture is centrifuged and the supernatant fluid removed; if the leucocytes alone are used centrifugation is not necessary. When the grafting is being done, the recipient area is washed with saline and dried with gauze. Grafts of any thickness can be used. The graft is turned upside-down on a piece of gauze. It is not washed. With separate camels'-hair brushes the under side of the graft and the recipient area are painted with cell extract and plasma respectively and the graft is fitted on. The edges are carefully adjusted; if desired the graft may be made slightly too large and its edges trimmed after it is in position. Light pressure with forceps causes the graft to adhere and a single layer of gauze is placed over it. No pressure is used. The results have been very successful: in the 10 cases reported the total area of skin grafted was about 100 square inches, of which less than 1 square inch failed to take. Time is saved at the operation as stitches are not required and the patient is fit for discharge within a few days.

Value of dried erythrocytes as surgical dressing.—Erythrocytes, superfluous in plasma preparation, have hitherto been discarded save for their occasional intravenous administration in suspension to patients lacking erythrocytes rather than plasma. Seldon and Young describe the value of erythrocytes as a surgical dressing, Moore and Unger having originated this use. The cells from a single blood group or of mixed groups after storage for a few days or weeks in a refrigerator form a gelatinous mass. This was used as a dressing for burns, ulcers and indolent wounds with gratifying effect but application was difficult as the semi-liquid

material escaped from the wound or was absorbed by the gauze dressing. Accordingly the gelatinous mass was dried to a fine powder applicable by dusting or by spatula, the Harper and Osterburg process being used. The powder is renewed daily or twice daily and the wound is covered with a dry dressing. Wounds, infected or perianal, occasionally become slightly malodorous. Three patients experienced pain from the application which necessitated its discontinuance; otherwise results although not uniform have been generally satisfactory. Three conditions illustrating the varied applicability of this dressing are cited: (1) a stump indolent after amputation through the thigh for arteriosclerotic gangrene, (2) the wide excision of an anal fistula and (3) a varicose ulcer of 8 years' standing.

Thrombin and fibrinogen in skin grafting.—The extensive use of blood plasma in military surgery renders thrombin and fibrinogen readily available. Their advantages as auxiliaries to skin grafting were studied by Cronkite, Lozner and Deaver at a naval hospital in 9 cases of burns and other injuries. Successful skin grafting requires a high level of haemoglobin, plasma protein and prothrombin and a good general condition; these are secured in preparation by a high protein diet, generous administration of vitamins A, B and C and, in order to maintain a normal prothrombin level, a sufficiency of vitamin K. Blood and plasma transfusion when necessary maintains a high standard of plasma protein and, with ferrous sulphate, of haemoglobin. Sulphanilamide ointment and pressure dressings and afterwards saline and chloroazodin (azochloramid) compresses prepare the recipient surface. The dried fibrinogen and thrombin are contained in phials ready for solution. The thrombin is applied by means of an atomizer. In the procedure adopted the recipient site was cleansed with ether and trimmed of exuberant granulations and scar tissue; haemorrhage was controlled by thrombin, pressure and elevation. Haemorrhage from the donor site was similarly controlled and sulphanilamide ointment dressings were applied after the grafts (free hand, simple pinch or split thickness) had been cut by means of the Padgett dermatome. The grafts were then dipped in fibrinogen solution and adjusted to the recipient defect. The area was then sprayed with thrombin and flooded with fibrinogen and a covering of Cellophane was applied at once with firm pressure. The Cellophane, dusted with 10 per cent sulphanilamide calcium carbonate powder, was covered by 10 layers of gauze saturated with glycerin containing 2 per cent sulphanilamide. Strapping over rubber sponges or cellucotton pads maintained pressure. The dressing was renewed on the third, fifth and seventh days and thereafter as required. The satisfactory results attained are attributed to the favourable recipient bed made possible by the use of thrombin and the close adhesion of the graft promoted by fibrinogen. Speed is fostered by the rapid control of haemorrhage and the diminution or abolition of suturing due to firm adherence.

Spanish or Florida moss as surgical dressings.—Moss, world-wide in its growth, has been used from time immemorial as a surgical dressing; it proved its worth in the Napoleonic and Franco-Prussian wars and, especially as sphagnum moss, in the war of 1914–18. Mayo and Wakefield emphasize its present value as a dressing and for padding splints, in regions where the growth or import of cotton is impracticable. Their present investigations concern a tree moss known locally as Spanish or Florida moss which grows along the eastern seaboard of the United States of America. Its absorbent power depends upon the leaves, which are built up of hollow cells, and therefore only the most richly leaved specimens are collected. Handling throughout collection and preparation should be reduced to the minimum since absorbent power diminishes with the breaking up of the moss. Slow drying at summer temperature minimizes its brittleness and preserves its softness and elasticity. Tests showed that Florida moss, packed in known weight in muslin bags, absorbed from 6 to 10 times its dry weight of water; it thus compares favourably with cotton which absorbs from 4 to 6 times its own weight. Well-dried moss can be sterilized by the methods applicable to cotton-wool and gauze dressings under like conditions.

Injuries of the heart

Disorders of rhythm.—Direct violence or strain may cause traumatic lesions of the heart. Barber describes the disorders of rhythm which may follow heart trauma as (1) auricular fibrillation, (2) bradycardia and (3) other forms of arrhythmia. The trauma may cause angina of effort. Coronary thrombosis after injury is rare but has been recorded. If a haemopericardium develops there are signs of heart tamponade which include shock, distended veins and distant heart sounds. Myocardial injury may be an unsuspected complication of other chest injuries and its existence can be ascertained by the electrocardiogram. Rupture of the heart or of the valve is rare. The existence of primary cardiac overstrain is much debated. If, after strain, there is dyspnoea, palpitation and praecordial discomfort, full investigation should be made, including radiographical examination. This will prevent a neurosis from developing, because the patient can be told at once whether or not his symptoms have an organic cause. Pain after a strain may signify a neurosis, or the rupture of a muscle fibre or a costo-chondral cartilage. The question of monetary compensation is an additional reason for caution in prognosis and for full investigation of the case.

Injuries of the peripheral nerves

Surgical repair.—Coleman discusses the surgical treatment of peripheral nerve injuries. He considers that exploration of the paralysed nerve is often the only way to ascertain the existing condition. Delay due to infection plays a less prominent part since the introduction of sulphonamides but the compounds are not without a damaging effect upon exposed nerve trunks. Tinel's sign, as indicating regeneration, is unsatisfactory and misleading. Partial nerve

lesions with vasospasm and causalgia are benefited by injection of the paravertebral sympathetic ganglia. The presence of a neuroma in continuity raises a question difficult to decide whether the neuroma should be excised or the nerve merely freed from its bed of scar or from pressure caused by callous formation. In the primary treatment of a gunshot wound the endings of a divided nerve should be tied together in order to prevent retraction and to allow a more satisfactory suture to be made at a later date, if necessary. Difficulties in approximation may be overcome by choosing the best position for the limb, the transposition of the nerve, the gentle stretching of the nerve, the resection of a long bone or the transplantation of nerves. Clinical experience with nerve transplantation has been very disappointing but Coleman considers that there is a good field for the method in defects of small nerves, such as the facial nerve and those of the hands. Union of nerve endings by a coagulated plasma cuff, as used in some experiments on animals, might prove valuable if combined with suture. The only satisfactory method is direct suture of healthy nerve endings. Fine interrupted silk sutures (as preferred by the author) or tantalum wire are suitable; the latter are visible in X-ray examination. Rotation of the nerve trunks should be prevented and scar tissue removed from the neuromatous ends. Haemorrhage from the cut endings is controlled by wet cotton pads or by application of a muscle graft. The author deprecates the use of wrapping material round the suture, but the nerve should be placed in a muscle bed. After a suture, the limb is placed in the position allowing the maximum relaxation of the nerve and is kept in plaster of Paris. Massage and the splinting of paralysed muscles play an important part. Even accurate alignment of nerve endings may not prevent the straying of downgrowing nerve fibres.

Effect of sulphonamides on healing.—In order to determine the effect of the use of sulphanilamide, sulphathiazole, sulphapyridine and sulphadiazine on an injured peripheral nerve and its adnexa, experiments were made on 58 cats by Hammond, Nonidez and Hinsey. One sciatic nerve (the other being left as a control) in each animal was treated with 0.25 or 0.5 gramme of one of the powdered sulphonamide compounds in question, in operations involving simple nerve section, primary suture, and suture delayed for 5 days after injury. The animals were killed 2, 5, 10, 15 or 30 days after operation. It was found that these drugs, when applied at the site of injury to the nerve, had not any influence on the extent and character of nerve regeneration, although, if not rapidly absorbed, they may cause mechanical hindrance to the passage of regenerating fibres. They do, however, exert some purely local chemical influence on the invading phagocytes, which are atypical and karyorrhectic. A typical acute inflammatory reaction, probably due to the operative trauma, followed by fibrosis of repairs was shown by the cut nerve. The acute reaction subsided after 5 days, but up to 30 days after operation small groups of inflammatory cells were to be seen. The administration of sulphanilamide, which is rapidly absorbed, caused no foreign body reaction such as occurred after the use of the other sulphonamide compounds. Only enough of these to ensure antiseptics should therefore be used. The new nerve fibres were of small and medium size and passed down beside the old myelin sheath pathways, presumably in a schwannian syncytium or between the sheaths of the endoneurium. A definite schwannoma was not observed. The best prognosis was given by primary suture.

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INTELLIGENCE TESTS

See also B.E.M.P., Vol. VII, p. 209; Interim Supplement, No. 17*; and Cumulative Supplement, Key Nos. 757-760.

Principal uses of intelligence tests*Adjustment to army life*

Importance of psychological tests.—Steinberg and Wittman have studied two groups of patients in the American Forces, one, group A, consisting of 22 psychoneurotics, the other, group B, of 87 psychotics; for purposes of comparison a third, group C, included 158 normal men attached to a Medical Corps unit. The control individuals have apparently made a satisfactory adjustment to army life whereas the two other groups have failed to do so. The patients in groups A and B, before entering the Army, had not shown any obvious abnormality and apparently broke down under the stress of their new life. The average ages for the three groups were practically the same. The average length of service for those in the two mentally ill groups was 6 months, whereas for those in the control group it was 10 months; breakdown occurred in the former groups at periods varying from one day to 18 months. Inquiry showed that the number of jobs held in civilian life and the longest period for which any one job had been held averaged 6.2 and 1.5 years for group A, 10.1 and 9 months for group B, 3.8 and 3.2 years for group C. This confirms the view that the previous work record is helpful in estimating a man's probable power of adjustment to army life. The parental relations, particularly with the mother, were found to be significantly better in the normal group than in the other two groups, an equal affection for both parents being usual in the controls. The controls showed the best adjustments in early life and school life. The psychologically poor risk appeared to be the shy, self-conscious person who shuns social contacts and who has strong emotional reactions, feelings of depression and unworthiness and tendencies towards moodiness, flightiness and instability. It is suggested that standardized methods of psychological examination should be applied to recruits.

Selection of officers

Main criteria in America.—A short method of examination for selection of officers for the American Forces is based on investigations upon healthy, normal young men carried out by Heath, Woods, Brouha, Seltzer and Bock. Three tests are used, designed to show whether a man is physically fit, has qualities of leadership and can withstand hardship. They are as follows. (1) The man steps on and off a 20-inch high platform 30 times a minute for 5 minutes or until he is forced to stop by exhaustion. The pulse is then counted every half minute for 3½ minutes. The index of fitness is computed by dividing the duration of exercise in seconds by twice the sum of half-minute pulse rates during recovery. (2) The man is interviewed for 10 minutes in order to assess his personal qualities. (3) The degree of masculinity of the subject is determined by observation of the body build. A close correlation is observed between the results of the three tests. For example, all those men who scored over 90 for physical fitness had a strong masculine component, and on the results of the short interview 41 per cent of the group with strong masculine component were rated 'excellent'. Conversely, of those who scored less than 30 for physical fitness only 12 per cent had a strong masculine component and, on the results of the short interview, of the group with weak or very weak masculine component no men were rated 'excellent' for officership and 77 per cent were classed as 'doubtful' or 'poor'. The authors point out that, *mutatis mutandis*, similar tests could be applied for the selection of persons suitable for other occupations. The method is designed not to eliminate the medically unfit but to grade those who can be regarded as healthy.

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INTESTINAL OBSTRUCTION

See also B.E.M.P., Vol. VII, p. 221; and Cumulative Supplement, Key Nos. 761–775.

Obstruction of the small intestine*Causes*

Hernia of the jejunum through mesenteric gap.—Morlock and Gray describe an unusual case of intestinal obstruction. A girl of 16 years of age complained of attacks, which dated from birth, of epigastric distention, after which vomiting occurred. In earlier years the attacks had been separated by long intervals, but recently they had occurred more often; they were repeatedly precipitated by the eating of coarse food. The vomited material was large in quantity and contained bile. Food taken several days previously could often be recognized in the vomit. X-ray examination showed enormous dilatation of the duodenum. Operation disclosed that the first loop of the jejunum had herniated through a congenital opening in the mesentery and so produced incomplete obstruction.

Primary lymphosarcoma of the duodenal wall

Report of a case.—Bisgard and Cochran report on a case of neoplasm of the duodenum. The patient, a housewife aged 42 years, gave 9 months' history of pain in the back. Diarrhoea had occurred at the onset and once subsequently. She had had one attack of jaundice and occasional attacks of vomiting, and had steadily lost weight and strength. Seven months after the onset the abdomen had been explored elsewhere and a cholecystostomy had been done for a lesion involving duodenum and pancreas, supposed to be inflammatory and thought to have resulted from perforation of a duodenal ulcer. X-ray examination showed a cholecysto-

duodenal fistula. Laparotomy disclosed a grossly thickened duodenal wall which when opened revealed a large ulcerated area. Resection of the pyloric end of the stomach, most of the duodenum and the head of the pancreas was performed. The common bile-duct was ligated and the stomach was anastomosed to the gall-bladder and to the jejunum. The severed end of the pancreas was sutured to the distal end of the duodenum. A pancreatic fistula developed but closed spontaneously; convalescence was otherwise uneventful. The patient died 3 months later, probably from recurrence; necropsy was not done. The pathologist reported the presence of lymphosarcoma, thought to be primary, in the duodenal wall.

Malignant disease of the duodenum

Carcinoma

Radiological and operational findings.—Child reports on the case of a man, 57 years old, who was admitted to hospital with jaundice of a month's duration. Radiological examination did not show any abnormality of the stomach and duodenal bulb; the second and third parts of the duodenum were very irregular in outline and a mass was seen in the third portion. Operation disclosed carcinoma of the second part of the duodenum involving the ampulla of Vater and the head of the pancreas. Resection was performed and the following anastomoses were made: gastro-jejunostomy, end to side; pancreatico-jejunostomy, end to end; cholecysto-jejunostomy, side to side. The patient recovered from the operation.

Primary carcinoma

Review of the condition.—Primary carcinoma of the duodenum is reviewed by Howard who states that it is a rare disease, according to records in the literature. In the Mayo Clinic reports carcinoma of the intestine involves the small bowel in about 1·4 per cent of cases. Within the duodenum the periampullary region appears to be the site most often involved whereas the third (distal) section is less commonly affected. The anatomical features of the duodenum and the nature of the food contents probably explain the low incidence of its involvement by carcinoma. The aetiology of duodenal carcinoma remains obscure, but neoplastic change does not appear to be associated with ulcers or with polypoid conditions. Duodenal carcinoma usually occurs as a scirrhous growth in the third part of the duodenum causing obstruction; a polypoid type however is sometimes seen. The disease is more common in males. The early signs are vague and many suggest some gastric disorder or cholecystitis. Anaemia is a characteristic finding, the hypochromic and microcytic type being more usual than the hyperchromic and macrocytic. The tumour is seldom palpable but examination of the stools often demonstrates occult blood. Later, if obstruction occurs, toxæmia and dehydration become apparent. Jaundice is rare except in the late stages. Perforation of carcinomatous ulcers is also uncommon, but is occasionally the first clinical manifestation of the disease. Metastases occur late and chiefly involve the regional lymphatic glands. Radiology is of assistance in establishing the diagnosis. Other diseases which may present similar signs are malignant and benign pyloric obstruction, carcinoma of the head of the pancreas or of the gall-bladder and invading the duodenum, carcinoma of the papilla of Vater or of the common duct, peritoneal tuberculosis and other more rare conditions. The prognosis of duodenal carcinoma is bad unless surgical treatment is given early.

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Child, C. G. (1943) *Ann. Surg.*, **118**, 838.

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Morlock, C. G., and Gray, H. K. (1943) *Ann. Surg.*, **118**, 372.

JAUNDICE

See also B.E.M.P., Vol. VII, p. 261; and Cumulative Supplement, Key Nos. 779–788.

Toxic and infective hepatic jaundice

Spirochaetosis icterohaemorrhagica

Weil's disease associated with meningitis.—Although it was present in the 13 cases now recorded Clapper and Myers emphasize that jaundice is not invariably concomitant with Weil's disease and they further maintain that the occurrence of meningitis is insufficiently appreciated. In this series 3 patients displayed rigidity of the neck, Kernig's and Brudzinski's signs, headache and vomiting and one of them also manifested epileptiform convulsions with a cell count of the cerebrospinal fluid which soared to 990 cells per cubic millimetre. Another of the 3 did not show any abnormality of the cerebrospinal fluid except increased pressure. Of 8 other patients without clinical signs of meningitis, subjected to lumbar puncture, 7 showed an increased cerebrospinal cell count. Of these 5 showed an increase of globulin. The cerebrospinal fluid was yellow in 10 of these 11 patients and in 8 bilirubin was detected, this suggesting increased permeability of the diseased meninges. Pericarditis and auricular fibrillation in one patient and delayed auriculo-ventricular conduction in a second, although occurring at the height of the urea retention familiar in this disease, were attributed to the toxins of *Leptospira icterohaemorrhagiae*, cardiac involvement not being characteristic of uraemia in general. Four patients, each with exaggerated retention of urea, suffered from persistent hiccough which subsided with the subsidence of the blood urea. Eight of the patients displayed haemorrhagic manifestations. The haemorrhagic tendencies of Weil's disease remain unexplained. The prothrombin percentages although reduced did not reach a level sufficient to account for haemorrhage.

Catarrhal jaundice

Infective hepatitis and the oral hippuric acid test.—Gordon analyses the clinical findings in 168 cases of infective hepatitis which were admitted to hospital from the Middle East Forces during the nine months December 1941 to September 1942; he makes special reference to the value of the oral hippuric acid test in estimating the deficiency of liver function during the course of the disease and its recovery during convalescence. Typically the onset was sudden with marked gastro-intestinal symptoms, anorexia and nausea and abdominal pain in the mid-epigastrium or right hypochondrium. Vomiting occurred in severe cases. Initial shivering and frontal or retro-ocular headache were common. Temperature ranged from 100° to 102° F. and pulse from 80 to 90, dropping to from 50 to 60 with the advent of jaundice. Dark-coloured urine was noticed one or two days before the onset of the jaundice and biliruria was present for 14 days after the jaundice appeared. Enlargement of the liver about one and a half fingers-breadth below the costal margin occurred in half the number of cases and lasted for about a week. Jaundice was present in varying depth in all the cases and lasted from 15 to 35 days. Many of the cases were labelled as 'gastritis' or 'dyspepsia' before the jaundice appeared; the main diagnostic aid in the pre-icteric stage is the presence of bile pigment and bile salts in the urine. Relapses occasionally occurred and the recovery of full hepatic function was sometimes very slow. Immunity was not conferred by an attack; the reverse was rather the case. There is no true clinical division into catarrhal and necrotic types. The treatment consisted in the provision of a low-fat and high-carbohydrate diet and the giving of glucose twice or thrice daily and a small dose of magnesium sulphate in the early morning.

Differential diagnosis in jaundice**Clinical and laboratory methods**

White reviews the clinical and laboratory methods that were most efficacious in the diagnosis of 500 cases of jaundice. A short course of moderate to severe jaundice with marked loss of liver function was more often due to hepatocellular damage than to obstruction. Investigations did not confirm Courvoisier's law since the gall-bladder was palpable in only 9 of 29 cases of malignant obstruction of the common duct. A palpable spleen suggested hepatitis rather than tumour of the liver, and spider angiomas of the skin were found only in well developed cirrhosis. Peritoneoscopy was mainly of value in diagnosing cancer or cirrhosis by vision or biopsy. In differentiating between obstructive and hepatocellular jaundice more importance was attached to the absence of urobilinogen in the urine and of bile pigment in the faeces than was to the depth of the jaundice as judged by the tint of the skin or the icteric index. Metabolic and excretion tests were of significance only in the early stages and when taken in series. Sensitive examinations, such as the bromsulphthalein and hippuric acid excretion tests, were positive in all types of liver damage and had not any differential value. Early investigation for urinary diastase was of good service in the diagnosis of acute pancreatitis as a cause of jaundice. The amount of cholesterol ester in the blood, the prothrombin level and the changes in serum proteins were all inadequate aids. Necropsies proved that positive Kahn or similar reactions in jaundiced patients did not usually indicate syphilis of the liver. In deep jaundice the Graham test was not reliable owing to the poor excretion of the dye by the liver.

Clapper, M., and Myers, G. B. (1943) *Arch. intern. Med.*, **72**, 18.

Gordon, I. (1943) *Brit. med. J.*, **2**, 807.

White, F. W. (1944) *New Engl. J. Med.*, **230**, 344.

JOINTS, DISEASES AND DISORDERS

See also B.E.M.P., Vol. VII, p. 278.

Pulmonary osteoarthropathy**Aetiology**

Possibility of endocrine abnormality.—Fried presents 4 cases of chronic pulmonary osteoarthropathy in patients with bronchiogenic cancer, careful study of which in 3 cases produced data for the hypothesis that the disorder arises from a disturbance in the function of the organs of internal secretion. In case (1) there was an acromegalic appearance, tufting of the terminal phalanges of the fingers and toes, splanchnomegaly and atrophy of the testes, and the hypophysis showed pronounced hyperplasia of the eosinophilic elements. In case (2), a woman, the features were acromegalic appearance and tufting of the terminal phalanges of the fingers and toes, hirsutism, macroglossia, and thickening of the cranial vault. In case (3), a woman, monogloid features were present, with secondary male characteristics, a large cortical adenoma of the left adrenal gland, several adenomas of the thyroid gland and hyperplasia of the cells of the anterior lobe of the pituitary gland. Case (4) manifested acromegalic features, gynecomastia, several cortical adenomas of the adrenal glands, tufting of the terminal phalanges of the fingers and toes and X-ray evidence of enlargement of the sella turcica. In this disorder the tibia and humerus are more intensely involved than is the epiphysis. Both hyperostosis and osteoporosis are present, the latter predominating. The bones are thickened but not elongated. Soft tissues are also involved; considerable thickening of the skin and subcutaneous tissues of the hands and feet occur. Fried also refers to the part played by the lungs in the metabolism of certain fats and esters. He points out that whereas carbohydrates and proteins after absorption are carried to the liver directly, fatty substances are transported by way of the lymphatic glands and thoracic duct to the right side of the heart and to the lungs. The

author considers that the functions of the lungs, other than those of respiration, merit further study.

Hip-joint

Congenital dislocation

Aetiology.—In his presidential address to the American Academy of Orthopaedic Surgeons, Badgley discusses the aetiology of congenital dysplasias of the hip. The excellent results obtained in cases recognized and treated early testify against the existence of a primary inherent factor in the acetabulum tending to produce dislocation and suggest that the acetabular changes are secondary. The author quotes cases in support of the conception that a primary dysplasia of the hip is produced by abnormal anteversion of the head and neck of the femur. Anteversion normally increases during foetal life and diminishes after birth. Failure of the normal postnatal change in the axis of the head and neck may result originally in an anterior dislocation and the hypoplasia of the posterior margin of the acetabulum is then explicable as the result of pressure by the neck against the cartilaginous rim. That arrest of normal growth of the acetabular structures can be produced by faulty pressure is suggested by numerous observations on patients with congenital dislocation or arthrogryposis. The coxa valga so often observed in X-rays of congenital dislocation of the hip is illusory, the result of the anteversion. In many cases of congenital dislocation the original position of the head can be shown to be anterior and cure can be brought about by simple correction of anteversion by internal rotation and abduction. Additional evidence of the embryonic arrest of rotation of the foetal limb is provided by the true embryonically dislocated hip which is seen in the multiple deformities of arthrogryposis multiplex congenita, in which the primary displacement is usually anterior.

Lorenz's closed manipulative method.—Whiston describes the post-operative care of 48 patients with congenitally dislocated hips of whom 41 were treated by Lorenz's closed manipulative method, one each by the methods of Lange, Calot and Ridlon and 4 by open operation. The average period of observation was 12 years. After reduction by Lorenz's method the hip was maintained for a period averaging 4 months in a first position of abduction 90 degrees, flexion 90 degrees and external rotation. The second position approximating abduction 60 degrees, flexion 45 degrees and internal rotation was used when the plaster was changed, with or without anaesthesia. The average duration of the position was again 4 months. For 24 patients a third position of lesser abduction and flexion with increased internal rotation was employed. In 5 cases involving 7 femurs antetorsion of the femoral neck necessitated osteoclasis. The internally rotated femur was fractured just above the condyles and the distal fragment was rotated until the patella faced forwards. The anatomical result was only twice successful. Redisllocations some years later in 3 patients required shelving operations. Functional results which showed full range of motion and painlessness and stability of the hip (12 patients) are classified as excellent. Some limitation in range, painlessness and fair stability rated 16 cases as good. Fourteen cases in which the patient had pain after moderate activity or moderate instability in walking are classified as fair. The remaining 6 cases are designated poor. The condition was unilateral in 33 and bilateral in 15 cases. Children under 5 years of age, immobilized for over 10 months, showed the best results. The results of open operation showed one good, 2 fair (including a woman aged forty-four years) and one poor. Poor results were obtained by the methods of Lange and Ridlon and a fair result by that of Calot.

Badgley, C. E. (1943) *J. Bone Jt Surg.*, **25**, 503.

Fried, B. M. (1943) *Arch. intern. Med.*, **72**, 565.

Whiston, G. (1943) *Surg. Gynec. Obstet.*, **77**, 307.

KETOSIS

See also B.E.M.P., Vol. VII, p. 372; and Interim Supplement, No. 20*.

Treatment

Diabetic acidosis

Essentials of treatment.—A plan of management of diabetic acidosis is formulated by Foster, Lowrie and MacMillan, as follows. (1) Keep patient warm in bed and avoid exposure. (2) Record temperature, pulse, respiration and blood pressure hourly. Give caffeine sodium benzoate, 7½ grains half-hourly, if systolic pressure is below 100. If this fails, give saline intravenously. If severe shock is present give plasma or blood. (3) Obtain urine at once, if necessary by catheterization. Insert indwelling catheter if patient is comatose. Examine urine hourly. (4) Give saline enema and make sure rectum is clear. Wash out stomach if vomiting is troublesome. (5) Estimate blood sugar, carbon dioxide, non-protein nitrogen, chlorides and cholesterol. Determine blood group, do full blood count and Wassermann reaction. (6) Give at once 50 units of soluble insulin intramuscularly. Give further doses of 20 units hourly until urine is sugar-free. Then estimate blood sugar and carbon dioxide again. (7) After 4 hours begin giving 20 grammes of carbohydrate in solution every 2 hours by any route except the rectal. (8) Give saline, 1,500 cubic centimetres, subcutaneously immediately; repeat in 12 hours if fluid intake is below 3 litres. Give abundant fluid by mouth. (9) Give sodium bicarbonate or sodium lactate 4 per cent intravenously if blood carbon dioxide is below 15 per cent.

Foster, D. P., Lowrie, W. L., and MacMillan, J. (1943) *Amer. J. digest. Dis.*, **10**, 371.

KIDNEY, SURGICAL DISEASES

See also B.E.M.P., Vol. VII, p. 380; and Cumulative Supplement, Key Nos. 829-840.

Congenital abnormalities*Horseshoe kidney*

Report of a case.—Flynn describes a case of horseshoe kidney with hydronephrosis. The subject was a male of 45 years of age whose presenting symptoms were backache and frequency of micturition. There had been marked loss of weight, dizziness and slight headache. Physical examination did not show any abnormalities, the blood pressure was within normal limits and the blood urea was 66 milligrams per 100 cubic centimetres; the urea concentration was satisfactory and the specific gravity of the urine was 1020. An excretion urogram showed distinct ptosis of the right kidney and some rotation and marked disorganization of the left kidney. Cystoscopy was normal; there was marked reduction in the excretion of indigo-carmin solution from the left kidney and a retrograde pyelogram revealed gross left hydronephrosis. A few days later a left ureteric catheter was passed and left *in situ* for 2 days, when a further indigo-carmin test showed good concentration of the dye. At operation the left kidney was seen to be joined to the right by an isthmus; this was divided and a fibrous band was observed to cross in the angle between the pelvis and ureter; this appeared to be the chief cause of the obstruction. A Walters plastic operation was performed on the kidney pelvis and this was followed by a Cabot nephropexy. Subsequent indigo-carmin excretion studies showed excellent renal function and an excretion pyelogram revealed both kidneys to be functioning normally.

Calculi*Ureteral calculi*

Removal by ureteral corkscrew.—Ainsworth-Davis advocates that whenever a calculus becomes impacted in the lower fourth of the ureter treatment by instrumentation should be tried before resort is had to operation. The procedure consists in ureteric meatotomy followed by use of the Welland-Howard spiral stone dislodger modified to the author's design as a ureteric corkscrew. A confirmatory radiograph is taken shortly before instrumentation. The anaesthetic to be preferred is pentothal and afterwards gas and oxygen. The initial procedure is that of meatotomy and the engagement of the stone in the spiral mesh of the dislodger. Withdrawal of the corkscrew, tempered with extreme caution, occasionally draws the stone into the bladder forthwith. Usually it is wiser to empty the bladder and withdraw the telescope, catheterizing attachment and cystoscope sheath, leaving *in situ* only the corkscrew. The patient is then returned to bed. On his recovery from the anaesthetic a further radiogram is taken. Next, a small weight extension, under the patient's control in case of extreme discomfort, is attached to the distal end of the corkscrew. This gradual traction on the calculus ensures its passage into the bladder and in a few instances through the urethra. The results in a series of 20 cases are given. In 2 patients the stone was removed forthwith and in 3 patients after 48 hours of weight extension. In 6 patients a second attempt was successful. Eight patients passed the stone naturally within 3 weeks and one required operation, two attempts to pass the corkscrew having failed.

Treatment

With notes on aetiology.—Although much is known about the formation and the cause of urinary calculi their varied occurrence has not been satisfactorily explained (Doherty). Most urinary calculi are formed in the kidney but they may be formed in the bladder if a foreign body provides a nucleus. The causes of urinary calculi may be divided into two main groups: factors outside the urinary system and factors confined to the urinary system. In the first group possible factors are the geographical district, diet, lesions of bone, hyperthyroidism and hyperparathyroidism and constitutional tendency. In the second group the factors are stasis and infection. Treatment is considered both when the presence of a stone in the urinary tract has been diagnosed and when a stone has been passed or surgically removed. If stones are shown by X-ray to be still present in the renal pelvis after an attack of colic an attempt may be made to wash them out. The patient should drink a large quantity of fluid and then lie on a bed the foot of which has been raised 3 or 4 feet from the ground. If the stone continues to give trouble surgical removal should be considered. Unilateral and bilateral staghorn calculi are treated by nephrectomy. When a stone is seen at the upper end of the ureter it should be left and the patient should drink much and should take exercise. If after several weeks X-ray shows little or no progress resort should be had to surgery. The treatment of bladder stones by crushing or by surgical removal should be combined with treatment of the cause. After its removal Doherty recommends chemical analysis of the stone, a complete urinary tract examination and the treatment of any obstructive or inflammatory lesion found. Diet, including the drinking of a large quantity of water, is important and Higgins has developed a high vitamin A acid ash diet which has strikingly reduced the incidence of, and in many cases has led to the dissolution of, recurrent phosphatic stones.

Tuberculosis*Diagnosis*

Occurrence of secondary bacteriuria.—It is known that the old belief that in all cases of renal tuberculosis there is sterile pyuria, is false. When Corbitt reviewed published work he found

that it was not stated whether the urine in which secondary organisms were found in association with tubercle bacilli came from the bladder or consisted of catheter specimens from the renal pelvis. The Mayo Clinic in the past 10 years has dealt with 775 cases of tuberculosis of the kidney, and 213 of these had the following criteria. (1) Catheterized ureteral specimens of urine had been collected. (2) Gram's stain, culture, or both had been done on these specimens. (3) Positive evidence of renal tuberculosis had been demonstrated. Of these 213 cases, secondary bacteriuria in the catheterized renal urine was found in 62 cases (29 per cent). The organism most commonly found was *Escherichia coli* which was present in 40 per cent of positive cultures. *Pseudomonas* was found in 23 per cent of cultures. In almost every case of secondary bacteriuria of the kidney there was also secondary bacteriuria in the bladder. In cases of unilateral renal tuberculosis, however, only the diseased kidney had secondary bacteriuria; this showed that tuberculosis was the primary infection. Gram positive stains were more frequent than were positive cultures. It is important to exclude tuberculosis in all cases of persistent urinary infection and not to be misled by secondary bacteriuria.

Tumours

Clinical picture

Sarcoma.—Weisel, Dockerty and Priestley¹ point out that, apart from their different age incidence, Wilms's tumour and sarcoma of the kidney have similar clinical signs and respond to the same treatment. They have made a special study of 35 renal sarcomas removed at the Mayo Clinic. Nineteen of the tumours were in males and 16 in females and ages ranged from 2½ years to 76 years. Two cardinal symptoms were abdominal mass and colicky pains. There was general weakness and malaise. Gross haematuria was present in 9 cases. Four of the patients had temperatures above 101° F. and 10 had a high blood pressure. The blood picture was that of secondary anaemia in 11 cases; in 10 there were large leucocyte counts. Urine analysis showed presence of albuminuria and of haematuria. Radiographs showed renal tumour in 17 cases. Nephrectomy was performed in 31 cases and exploration with biopsy in 4. The 31 specimens of renal sarcoma were all unilateral and varied in length from 44 centimetres to 4 centimetres. The greater number of the tumours consisted of spindle cells resembling fibroblasts and they were therefore called fibrosarcomas. A few of the tumours had some myxomatous degeneration and were called myxosarcomas. Three tumours were classified as leiomyosarcomas; they probably originated from the smooth muscle elements of the renal pelvis or renal capsule. One tumour was a rhabdomyosarcoma. Three were a mixture of liposarcoma and fibrosarcoma and were probably derived from the renal capsule. One had the characteristics of lymphosarcoma but as there is no lymphoid tissue in the kidney the tumour was regarded as a peculiar localization of otherwise generalized lymphosarcomatosis. All these renal sarcomas were of great malignancy and grew rapidly; there was early and widespread metastasis. Early radical removal of an affected kidney together with the tumour is the treatment of choice.

Wilms's tumour

Clinical commentary.—In analysing the records of mixed renal tumours treated at the Mayo Clinic from 1904 to 1940, Weisel, Dockerty and Priestley² have admitted as Wilms's tumours only those exhibiting carcinoma-like cells in tubular, cylindrical, papillary or solid arrangement with spindle-shaped sarcoma-like cells. Other tissues, especially striated muscle, were detected in many instances. Forty-four cases showed the essential characteristics: 36 patients were under 9 years old and 8 ranged in age from 12 to 59 years. The tumour, always unilateral, affected females twice as often as it did males. From innumerable theories of origin 3 possibilities are acceptable to the authors, namely (1) the embryonic cellular rest, (2) the teratomatous development of one or more germ layers or (3) the perverted growth of the renal mesenchyme. A rapidly growing abdominal mass and rapidly deteriorating health were almost invariable symptoms and fever occurred in one-half of the number of patients. Severe pain accompanied the passage of renal clots but pain generally was dull and infrequent. Haematuria was present in one-third of the number of patients but was severe in 5 instances only. Neither X-ray irradiation alone nor nephrectomy alone offer great hope of success in treatment. Nephrectomy, immediate when practicable, with subsequent X-ray irradiation is the best procedure. If irradiation before operation is employed, such employment should aim only at reducing the tumour to operable dimensions and the period of its application should not exceed 3 weeks. Irradiation should be resumed after operation. Prognosis is very grave. Thirty-one patients died within a year of operation. Six more succumbed within 4 years. Seven are living after periods of from 2 to 20 years.

Radiological aspect.—In Wilms's tumour, the most frequent renal neoplasm of childhood, rapid growth is more prevalent than haematuria and pain. Rowe and Frazer illustrate the radiological aspect by 4 cases. Adrenal tumours, sarcoma involving the retroperitoneum or bowel, congenital abnormalities of the kidney, mesenteric and pancreatic cysts or splenic enlargements require consideration in differential diagnosis. Youth may prevent cystoscopy with retrograde pyelography. When intravenous urography is not feasible, an intramuscular injection of diodrast (diodone) in 35 per cent solution is employed. Irradiation alone, nephrectomy alone and nephrectomy before or after irradiation have had their advocates, but both pre-operative and post-operative irradiation are recommended by the authors. Ladd and White, who oppose this last method, deprecated operative delay and obtained 14 probable cures in 60 cases. Four advantages attend pre-operative irradiation. (1) The reduction of the tumour

minimizes operative manipulation; (2) the production of fibrosis diminishes vascularity; (3) the patient comes to operation in good condition; (4) the rapid response of these tumours to irradiation confirms diagnosis. In the first case now reported pre-operative irradiation was not employed. Death from pulmonary metastases ensued 5 months after operation. The second and fourth cases received irradiation of approximately 4,000 r during a fortnight. Nephrectomy ensued within 6 weeks and a month later irradiation was resumed for 17 and 10 days respectively. Both patients survive in good health after the lapse of 4½ years and 7 months respectively. In the third case a fall 3 days before admission, initiating continuous abdominal pain and vomiting, preceded diagnosis and poor condition delayed operation but after similar courses of irradiation the patient survives in good health 2 years later.

Ainsworth-Davis, J. C. (1943) *Brit. J. Surg.*, **31**, 34.

Corbitt, R. W. (1944) *J. Urol.*, **51**, 11.

Doherty, W. D. (1943) *Practitioner*, **151**, 341.

Flynn, R. (1943) *Aust. N.Z. J. Surg.*, **13**, 138.

Rowe, E. W., and Frazer, M. D. (1944) *Radiology*, **42**, 107.

Weisel, W., Dockerty, M. B., and Priestley, J. T. (1943)¹ *J. Urol.*, **50**, 399.

— — — (1943)² *ibid.*, **50**, 564.

LABOUR: NORMAL LABOUR

See also B.E.M.P., Vol. VII, p. 417; and Cumulative Supplement, Key Nos. 841–844.

Phenomena of normal labour

Duration of labour

Effect of salt-poor diet.—The effect of a salt-poor diet on the length of labour is investigated by Schuitema. A group of 50 patients voluntarily adopted a rigidly controlled salt-poor diet for periods varying from 4 to 19 weeks before parturition and another group of 50 patients was observed as a control. The average duration of labour in the first group was then compared with that of the second. All the patients were primiparae; all came from similar environments and received the same antenatal care from the same doctor. Chloride determinations were made weekly on 24 specimens of urine. Only cases of normal delivery were included in the analysis of results and all the labours were spontaneous in onset. The average gain in weight during pregnancy was comparable in both groups; the control patients gained 23·2 pounds and the salt-poor group gained 21·4 pounds. The average age in the control group was 18·2 years and in the salt-poor group 19·2 years. It was found that in the latter group the average length of labour was 1·74 hours shorter than that of the control patients and there were smaller variations in the length of labour. It is pointed out that text-books state the average duration of labour in primiparae to be 18 hours and in multiparae to be 12 hours but it is apparent that the duration of normal labour in both primiparae and multiparae is considerably less than these figures indicate. The tendency for labour to be shorter with greater salt restriction and with increasing duration of the salt-poor diet suggests that there might be a considerable decrease in the length of labour with a true salt-poor diet.

Conduct of normal labour

Prevention and repair of lacerations

Optimum conditions for perineorrhaphy.—Malpas points out the frequency with which patients, in whom a complete tear has occurred and has been repaired within 24 hours under conditions of general practice, show an unsuccessful outcome: the repair breaks down within a fortnight. The usual recommendation is to defer secondary repair for at least 3 months, but the author has employed or seen early resuture in 6 cases with satisfactory results. In 5 of the cases a complete breakdown had occurred, whereas in the remaining one the breakdown was partial and a recto-vaginal fistula was present. Repair was carried out between 7 and 28 days after delivery. Two of the cases were pyrexial from uterine infection. Every tear healed well and within 2 weeks. No special technique is called for. Malpas considers that the primary failure is often due to poor operating conditions. Many of the failures would be avoided if it were the rule to defer the primary repair of complete tears for from 12 to 24 hours after delivery until better conditions and perhaps better assistance could be obtained.

Malpas, P. (1944) *Brit. med. J.*, **1**, 590.

Schuitema, D. M. (1943) *Amer. J. Obstet. Gynec.*, **46**, 707.

LABOUR: FAULTS IN THE FORCES

See also B.E.M.P., Vol. VII, p. 445.

Inefficient uterine contractions

Treatment

Experiments with gorse infusion.—An infusion of gorse (*Ulex gallii*, common furze or whin) is traditionally administered in the North of England for the purpose of expelling the cow's retained placenta. Having witnessed the effect Smith and Wilson prepared several extracts of gorse which yielded concentrates of equal potency. These were pooled into a stock concentrate denominated S. In guinea-pigs, S, 1 in 1,000, caused tonic contraction of the virgin uterus which lasted for 2 minutes. Oestrus so sensitizes the uterus that a dilution of 1 in 10,000

produced contraction and 1 in 200 prolonged contraction up to a period of 20 minutes. Pregnant uteri reacted similarly but sensitivity varied, depending probably upon the period of gestation. In contrast the parturient uterus showed brief contraction and then prolonged relaxation. These effects were uninfluenced by atropine and did not modify the response to adrenalin. A single intravenous administration of S, 0.2 millilitre, produced similar response in the virgin cat's uterus, with a transient fall of blood pressure, probably due to impurity, and then a sustained rise. Twelve tests on isolated parous human uteri were then made. To a concentration of S, 1 in 60, 2 pregnant human uteri responded with vigorous contraction but relaxation did not ensue. In the 10 non-pregnant human uteri relaxation of various degree ensued after brief contraction. Of the 10, 2 pre-ovulation specimens showed the greater sensitivity. A cow's pregnant uterus gave results comparable to those in the human being. Experiments on rabbits were indecisive. A bitch resembled the guinea-pigs in reaction but required higher dosage. Experiments in toxicity made in mice suggest bronchial spasm as a danger. Pharmacological research is necessary to exclude the presence of more than one active principle. Satisfactory methods of extraction may provide a valuable oxytocic from the readily available *Ulex gallii*.

Smith, W., and Wilson, A. (1943) *Brit. med. J.*, 2, 322.

LABOUR: MALPOSITION AND MALPRESENTATION OF THE HEAD

See also B.E.M.P., Vol. VII, p. 451; and Cumulative Supplement, Key Nos. 848-853.

Face presentations

Course and prognosis

Importance of radiology and pelvimetry.—From analysis of the Harlem Hospital, New York, records of 28 years Posner and Buch deduce that one in 529 deliveries is a face presentation and one in 3,543 is a persisting brow presentation. Of the 16 known predisposing factors, the following were found in this series of cases: contracted pelvis, large child, monstrosity, hydramnios, abnormal placental implantation and coils of cord around the neck. The face presentations occurred after external version had been carried out. In 41.8 per cent of cases none of these causes was operative. Multiparity and large infants as predisposing factors to face presentation are attributed to the increasing birth weight of children born in successive pregnancies to the same mother. Diagnosis by abdominal palpation alone before labour is rarely possible. In 54 patients vaginal and rectal examination shortly after rupture of the membranes reached successful diagnosis in 18 cases. Later the large caput succedaneum increases difficulty and rectal or vaginal diagnosis during the second stage was reached only 11 times. The early employment of radiology, with pelvimetry, is therefore strongly advocated. The treatment recommended in presentations of the mentum anterior and transverse order is non-interference so long as progress continues since 3 deliveries in 4 ensue spontaneously. Caesarean section is employed for the mentum posterior presentation if it is diagnosed either before labour or after labour's onset if the os is undilated and the condition of mother and foetus is good. It is considered that a wider employment of Caesarean section, especially in primiparae, would reduce maternal and infantile mortality.

Posner, A. A., and Buch, I. M. (1943) *Surg. Gynec. Obstet.*, 77, 618.

LABOUR: BREECH PRESENTATION

See also B.E.M.P., Vol. VII, p. 470.

Treatment

Complications

Breech presentation in primiparae over thirty-five.—Walsh and Kuder present a study of breech presentation in 55 primiparous mothers over 35 years old who were delivered in the course of 10 years at the New York Hospital. Among elderly primiparae the incidence of breech presentations was 6.76 per cent, whereas throughout nearly 30,000 deliveries during that period it was 4.72 per cent. Of these 55 patients 40 were pregnant for the first time and 15 had experienced induced or spontaneous abortion. In 3 of 4 sets of twins the first infant only presented the breech. Both infants offered breech presentations in the fourth case. Two patients only had calculated the date of delivery correctly, 34 were correct within a fortnight; of the remainder 16 were delivered by Caesarean section. Compared with the entire clinical material significant prevalence of contracted pelvis or ante-partum complications was not shown, except that myoma uteri showed an incidence of 7.2 per cent as contrasted with the general incidence of 1.9 per cent, and that toxæmia showed 14.4 compared with 11.2 per cent. Other differences comprised a prolonged labour exceeding 30 hours in 21.8 per cent compared with 9.9 per cent among the total cases, and premature rupture of the membranes in a percentage of 40 compared with 36. A maternal mortality of 3.6 per cent, contrasted with a general mortality of 0.198 per cent and an infantile mortality of 12.5 per cent, emphasize the dangers of breech presentations. The notable number of 16 Caesarean deliveries were compelled principally by disproportion of pelvis and infant—especially when overdue—by myomas and by premature rupture of the membranes.

Walsh, J. W., and Kuder, Katherine (1944) *Amer. J. Obstet. Gynec.*, 47, 541.

LABOUR: COMPLICATIONS OF THE THIRD STAGE

See also B.E.M.P., Vol. VII, p. 523.

Inversion of the uterus*Treatment*

By conservative methods.—Burwig discusses the conservative treatment of acute uterine inversion. The condition of acute puerperal inversion of the uterus is comparatively rare; the author presents reports of 4 cases. Mismanagement of the third stage of labour has been stressed as a causal factor. If shock is absent the inversion should be treated at once but otherwise shock must first be treated promptly and effectively. Opinions are divided between conservative and operative treatment. The author's 4 cases had a successful outcome. One patient had neither shock nor haemorrhage; she was at once deeply re-anaesthetized and the inversion of the uterus was corrected by manipulation. In the other 3 cases shock and haemorrhage were present; manipulation was therefore delayed until the patient had recovered. In the author's technique, haemorrhage is controlled by firm packing of the vagina against the inverted fundus and transfusions are administered. Some form of ergot may be given to hasten involution and sulphonamides are presented to guard against infection. About one week *post partum*, under combined spinal and inhalation anaesthesia, the inversion is corrected by taxis, for example squeezing the fundus as one would a rubber ball held in the palm of one's hand. The uterine cavity may or may not then be packed to prevent re-inversion of the uterus. Of the 4 cases reported on, 2 patients were subsequently delivered of another infant without any abnormal incident.

Burwig, J. (1944) *Surg. Gynec. Obstet.*, **78**, 211.

LABOUR: OPERATIVE AND MANIPULATIVE PROCEDURES

See also B.E.M.P., Vol. VII, p. 533.

Version*External version*

In seventh and eighth month of pregnancy.—Trubkowitch and Archangelsky analyse 324 instances in a Moscow Clinic of prophylactic external cephalic version performed during the thirty-fifth and thirty-sixth week of pregnancy under anaesthesia in only 4 cases. Success was attained in 251 breech and in 42 transverse or oblique presentations. In the remaining 10 per cent of cases, version was unattainable or the original position recurred. As the first manipulation was usually successful repetition of the procedure was rare. Comparison with a foetal mortality of 0.94 per cent for vertex presentations in nearly 108,000 deliveries showed that successful prophylactic version reduced the mortality of breech and of transverse or oblique presentations to the same level, which was a 10-fold reduction for breech and a 25-fold reduction for transverse and oblique presentations. The hypothetical complications of version proved to be non-existent. It did not predispose to premature labour. Neither adherence nor premature separation of the placenta was encountered and a solitary case of slight haemorrhage which occurred 3 weeks before labour had no untoward effect. Early rupture of the membranes occurred more rarely, not more frequently, than usual. Finally, the occurrence of prolapse or twisting of the cord was, after version, as rare as it was in ordinary vertex presentations. The authors state that when the indications and contra-indications are observed and the correct technique is carried out the procedure is without danger.

Caesarean section*Classical operation*

One hundred cases in a rural hospital.—Vickers reports on 100 cases of Caesarean section in a rural hospital in the United States of America. There was no maternal mortality. The patient was prepared as usual for operation but was not given sedatives during the few hours immediately before operation as it was believed that they contributed to the occurrence of foetal asphyxia. The anaesthetic given was usually nitrous oxide-ether. The uterine incision was made fairly low, but was higher than the low cervical incision; the baby was extracted by the feet. Post-operatively a tight Scultetus binder was worn which prevented intestinal distention and gave great comfort. Caesarean section may be indicated in cases of disproportion, in placenta praevia if the child is living and the mother is a good risk, in selected cases of toxæmia and in cases of separation of the placenta with much haemorrhage. The fact that a Caesarean section has been done once is usually an indication that it should be performed in the next pregnancy, although the second child is sometimes delivered normally per vaginam. Intercurrent disease, for example tuberculosis, may also be an indication for the use of the procedure. The operation should be avoided if the patient has been long in labour, if she has had many pelvic examinations or a trial labour or if she has pyrexia on admission to hospital. In the border-line case labour may be allowed to start or the membranes to rupture but the author has found that rise of temperature post-operatively corresponded to the previous duration of labour and therefore the decision to perform Caesarean section had to be made quickly. The giving of sulphonamides have lessened the risks in the author's series of operations.

Trubkowitch, M. V., and Archangelsky, B. A. (1944) *Brit. med. J.*, **1**, 220.

Vickers, D. M. (1944) *Amer. J. Surg. N.S.*, **63**, 168.

LABOUR: ANAESTHESIA AND ANALGESIA

See also B.E.M.P., Vol. VII, p. 573; and Cumulative Supplement, Key Nos. 895 and 896.

Anaesthesia and analgesia*Methods of administration*

Gas and air analgesia.—Minnitt gives an account of the history and progress of gas and air analgesia in obstetrics. Gas and air analgesia was first used in the United States of America by means of the machine devised by McKesson and in 1933 the McKesson apparatus was adapted in England for use in labour. A mixture of gas and air was inhaled intermittently by the patient and the results of various trials were found to be very satisfactory. Considerable relief from pain was obtained in 92.8 per cent of cases and the gas and air could be administered for several hours. The compact Queen Charlotte model was designed for convenience and portability. It is most important that the patient should receive antenatal instruction on the use of the apparatus so that she can cooperate properly when labour begins. The timing of the inhalations must also be carried out properly if the optimum effect is to be obtained; a special attachment enables pure gas to be inhaled for 2 or 3 breaths, inhalation thereafter being of the standard gas and air mixture. This method provides adequate analgesia without cyanosis. In the first stage of labour the gas and air must be inhaled for a sufficient time to produce adequate saturation of the blood before a pain begins and in the second stage the mixture must be inhaled between the pains so that expulsive efforts are not weakened. The periods of rest between the pains help to conserve the patient's strength and amnesia is achieved. The analgesia may be increased by the admixture of other anaesthetic drugs, using a Rowbotham's bottle connected to the McKesson apparatus. It is advocated that midwives should have adequate training in obstetric analgesia, that the present rules regarding administration of anaesthetics by midwives should be modified and that there should be depots from which machines ready for use could be obtained by midwives.

Caudal anaesthesia and management of complications.—Gready draws attention to the hazards which accompany the use of caudal anaesthesia in obstetrics and suggests methods for avoiding or dealing with them. The worst disaster that can happen, he states, is massive spinal anaesthesia after subarachnoid injection. The precautions essential to its avoidance are the aspiration test and the test dose. When aspiration has proved by the absence of spinal fluid that the dural sac has not been entered a test dose of 8 cubic centimetres of a 1.5 per cent solution of metycaine (γ -(2-methylpiperidino)-propyl benzoate hydrochloride) is injected and its effect is watched for 10 minutes before the completion of the injection is proceeded with; this is effected by giving 30 cubic centimetres of a 1 per cent solution of procaine hydrochloride. This procedure should be repeated before each subsequent injection is given. When disaster follows neglect of such precautions immediate withdrawal of 100 cubic centimetres of cerebrospinal fluid should be made while the patient is being supported in the sitting position. Artificial respiration and measures to combat shock will be required. Infection inside or outside the sacral canal ranks next in gravity. A faultless technique is the obvious prevention, but in the event of infection the treatment is that for surgical infection in general. Laminectomy may be necessary. The intravenous injection of procaine hydrochloride is 10 times more toxic than is its subcutaneous injection. Again, aspiration and the small preliminary injection afford great although not absolute protection. Since the barbiturate drugs greatly increase resistance to the toxic effects of cocaine derivatives they may be relied on for the immediate control of convulsions. Certainly barbiturate solutions should be at hand; in some cases they may be used in premedication for this type of anaesthesia. Idiosyncrasy may be suggested by a history of severe reaction at a dental extraction. Should convulsions occur in such a patient a barbiturate drug intravenously administered will control them but for the true anaphylactic reaction an immediate hypodermic injection of adrenalin is necessary. A fall in blood pressure is usual but it is not significant. In 27 of 121 patients a fall of over 20 millimetres of mercury occurred, associated always with anaesthesia at or above the umbilicus. The hypodermic administration of ephedrine, with oxygen inhalations, was invariably effective.

Continuous caudal anaesthesia.—In a series of 200 obstetrical cases the patients were given continuous caudal anaesthesia by Lyons and Hansen with success in 195 cases. Contra-indications are (1) any infection around the sacral area, (2) hypersensitivity to local anaesthetics, (3) sacral or other spinal abnormality, (4) abnormal mental state. Anaesthesia is started when the cervix is dilated to 3 centimetres and contractions are long and occurring often; the needle is removed when the patient is taken to the delivery room. Premedication with barbiturates reduces toxicity. Metycaine was the drug used in all cases for caudal anaesthesia. The dangers are (1) intravenous or subarachnoid injection of the drug, (2) infection at the site, (3) breaking of a needle, (4) a fall in blood pressure, (5) toxic signs and (6) trauma to the sacrum. The authors did not meet with any obstetrical complications which would contra-indicate the use of caudal anaesthesia, except an increase in the number of operative deliveries needed in vertex presentations.

In a paper given at a meeting of the New York Obstetrical Society, Lull discusses the use of continuous caudal analgesia, on the basis of his records of 927 obstetrical cases. He emphasizes the importance of the careful selection of patients. He considers caudal anaesthesia to be of great value in cases of cardiac disease, upper respiratory infections and premature labour.

It has been successfully used in pre-eclamptics as well as in eclampsia. Better results appear to be found in patients of higher mentality. Lull estimates that 62 per cent of patients are suitable. He considers it essential for success and for the safety of mother and child that caudal anaesthesia should be given only by trained and skilled obstetricians and anaesthetists in a well equipped maternity hospital, with appliances at hand for any emergency. A pre-anaesthetic dose of a barbiturate is desirable, and quietness in labour and delivery rooms is essential. The anaesthesia should be started when the patient is having pains of 30–40 seconds' duration at 5-minute intervals, the cervix is 3 centimetres dilated, and the presenting part is engaged or fixed in the pelvis. A test dose of 8 cubic centimetres of metycaine is first given, followed 10 minutes later by 20 cubic centimetres every 40 minutes. The blood pressure and foetal heart tone must be checked often. More posterior positions and transverse arrests were found to occur, and it has been more often necessary to use forceps than in cases which were not given caudal anaesthesia. The placenta separates very quickly, because uterine muscle tone is especially good; the fundus requires only slight pressure. With this method of anaesthesia there is, according to the author, relief of pain, excellent condition of baby at time of birth, delighted mental attitude of the mother, minimal blood loss and easy termination of the third stage of labour. The mother is left in a good physical condition and does not show any signs of exhaustion.

Use of sedatives

Pethidine analgesia

Results in 150 cases.—The value of pethidine (1-methyl-4-phenylpiperidine-4-carboxylic acid ethyl ester) analgesia in obstetrics has already been studied both in Great Britain and in the United States of America. Gallen and Prescott describe the results obtained in 150 cases, of which detailed records were kept in 100 cases (70 primigravidae and 30 multigravidae). Oral administration was found to be unsatisfactory but two alternative dosage schemes of administration by intramuscular injection and by intravenous injection were used which conferred complete or adequate analgesia during the first stage of labour in 60 per cent of the patients. The drug was used in conjunction with chloral hydrate, potassium bromide and tincture of opium or with scopolamine (hyoscine); the first dose was given when the cervix was so dilated as to admit 2 fingers and when the patient was having regular pains. Intravenous injection had a more rapid effect than had intramuscular injection but the latter method of administration was found to be equally effective. Analgesia was produced within from 5 to 15 minutes and continued for 3 or 4 hours. Labour appeared to be longer than that in a control group of patients who were given only the stock mixture containing chloral hydrate and potassium bromide but the apparent effect may have been due to the fact that a number of apprehensive patients were among those who were treated with pethidine. The actual duration of labour in both primiparous and multiparous patients did not exceed the average times. There was not any increase in complications and 91 per cent of the babies were normally active after delivery. Toxic manifestations occurred in about 28 per cent of the mothers and included vomiting, a transitory rise in blood pressure, dizziness and vertigo and tingling in the limbs. Spitzer also reports on the use of pethidine in labour; he used the drug in 80 cases of normal labour and found that after oral administration 90 per cent of the patients obtained relief lasting from 1 to 4 hours. The duration of normal labour was reduced and there were no serious harmful effects. Five babies were slightly asphyxiated after delivery and there were 2 cases of post-partum haemorrhage. It is considered that pethidine is a useful antispasmodic drug for conferring analgesia during labour but that intravenous injection is contra-indicated in cases of toxæmia and hypertension. The relatively wide margin of safety of pethidine in normal cases enables repeated doses to be given and its use entails less risk to the infant than does that associated with morphine.

Gallen, Bedelia, and Prescott, F. (1944) *Brit. med. J.*, **1**, 176.

Gready, T. G., Jun. (1943) *J. Amer. med. Ass.*, **123**, 671.

Lull, C. B. (1944) *Amer. J. Obstet. Gynec.*, **47**, 312.

Lyons, H., and Hansen, F. M. (1944) *Amer. J. Obstet. Gynec.*, **47**, 105.

Minnitt, R. J. (1943) *Proc. R. Soc. Med.*, **37**, 45.

Spitzer, W. (1944) *Brit. med. J.*, **1**, 179.

LABOUR: RADIOLOGY

See also B.E.M.P., Vol. VII, p. 584; and Cumulative Supplement, Key Nos. 897–908.

Introduction

Information available

Use of radiology in obstetric prognosis.—Hartley believes that close collaboration between obstetrician and radiologist can produce a remarkable degree of accuracy, with regard both to observation of facts and to prognosis concerning delivery. The practitioner who refers cases to the radiologist should state what his particular problem is and what information he hopes for, and should give all relevant details. Radiology can produce almost invariably accurate information in the following instances. (1) Detection of the foetus—possible in favourable circumstances at about the tenth week of pregnancy. Multiple pregnancies can nearly always be distinguished from hydramnios. (2) Estimation of duration of pregnancy.

(3) Foetal death: overlapping of the vault bones of the skull and the rolling of the foetus into a ball are usually sufficient to demonstrate this. (4) Presentation and position of the foetus. (5) Gross abnormalities of the foetal skeleton such as anencephaly and spinal deformity. (6) Pelvimetry and cephalometry. The diameters of the pelvic inlet can be measured accurately. (7) Pyelography. Even in advanced pregnancy, intravenous pyelography is not contra-indicated. In the following groups radiological methods can in expert hands give valuable information; this may be exact, but it usually comes within the category of an estimate or personal opinion. (1) Disproportion: its degree and the indication for trial labour, induction or Caesarean section. (2) Cause of non-descent of the foetal head near term apart from disproportion. (3) Placenta praevia, and its degree. The injection of sodium iodide in 12.5 per cent solution into the bladder, with the resultant radiographs, is of some value. (4) Complications of pregnancy and the differentiation between a pregnancy and an abdominal tumour. (5) Minor foetal deformities or defects. Radiology in pregnancy embraces a complete review of the abdomen, pelvis, uterus, and foetus.

Hartley, J. B. (1944) *Med. Pr.*, **211**, 186.

LARYNX DISEASES

See also B.E.M.P., Vol. VII, p. 612; Interim Supplement, No. 16*; and Cumulative Supplement, Key Nos. 918–927.

Surgical anatomy of the larynx

Vocal cords

Part played by extrinsic muscles in support.—One school of laryngologists holds that the extrinsic laryngeal muscles do not play a part in voice production. Sokolowsky agrees with the second school which affirms that the support of the extrinsic muscles is essential to the adductor action of the intrinsic muscles. Within this school there is dissension, Schilling having noted relaxation of the cords as a result of the action of the sternothyroid muscle, whereas Katzenstein in experiments on animals noted tension. Sokolowsky's patient, a singer with a mezzo-soprano voice, suffered loss of the higher notes after thyroidectomy. The recurrent laryngeal nerve was intact. The undulating edge of the vocal cord which is a characteristic of a paralysed cricothyroid muscle, was absent. The surgeon reported severance of the sternohyoid, sternothyroid and omohyoid muscles during thyroidectomy. This recalled the parallel case of a singer with a high soprano voice, reported by Katzenstein, in whom during thyroidectomy the sternohyoid, sternothyroid and thyrohyoid muscles were severed. If the sternohyoid and sternothyroid muscles, the severance of which was common to 2 cases, are alone considered, Katzenstein's observations on the result of their stimulation in dogs become relevant. In the first place he found that stimulation of these muscles produced tension of the cords; secondly the note produced by blowing upon the vocal cords through the trachea during stimulation of the laryngeal nerves, after the extrinsic muscles had been severed, was of lower pitch than the note obtained before severance was made. It is deduced that the extrinsic muscles provide a basis for the finer adjustments of the intrinsic muscles. As the speaking voice is unaffected and but few singers undergo thyroidectomy the problem has been little ventilated. Fortunately thyroidectomy without severance of these muscles grows in favour. Here, orthophonic exercises effected recovery of the lost range.

Acute laryngo-tracheo-bronchitis

Clinical picture

Effect of chemotherapy.—To judge from an address given by MacCready in New York, the change in the picture of acute laryngo-tracheo-bronchitis is chiefly due to the advent of chemotherapy. Prior to this, and since the pandemic of influenza in 1918, many of the reported cases were characterized by an overwhelming seriousness of obstructive symptoms which persisted to a fatal termination—even after tracheotomy—owing to the continued formation of tenacious inflammatory exudate farther down the bronchial tree in spite of all attempts at alleviation by instrumental and medicated measures. Three illustrative cases of this type are cited, all in young children who at first appeared to be suffering only from coryza or sore throat. In one of these in a matter of a few hours, acute oedema of the larynx gave a fatal result; investigation of the heart, blood and lungs yielded pure cultures of *Haemophilus influenzae* B. In 1941 one observer reported on 10 cases of acute laryngo-tracheo-bronchitis with septicaemia due to this organism. Four of the patients who were not treated with sulphonamides died, whereas those to whom they were given recovered. One patient who was intolerant to them was given antihaemophilus B rabbit serum and with such beneficial results that the observer thereafter combined it with sulphadiazine as routine treatment. A severe epidemic of influenza has not been experienced in the United States of America for several years, but it is stated that since 1941, in 73 cases of laryngo-tracheo-bronchitis all the patients who received adequate sulphonamide treatment recovered with the exception of one. Tracheotomy was necessary in 16 of the cases but subsequent obstructive exudate did not form in the trachea or bronchi. The mortality rate in pre-chemotherapy times is said to have exceeded 50 per cent on the average including epidemic years. It would seem from more recent investigation that the *H. influenzae* B is tending to replace in virulence the haemolytic streptococcus of the 1918 type of case.

Treatment

Convalescent serum in treatment.—Baum discusses the non-surgical aspects of the treatment of acute laryngo-tracheo-bronchitis, a very serious disease affecting children. He points out that presumably surgical intervention always will play a necessary part in treatment, at any rate in late or neglected cases, but that many patients can now be treated non-surgically. Acute laryngo-tracheo-bronchitis usually occurs during epidemics of respiratory disease; if the laryngeal respiratory obstruction is relieved in time by surgical methods the patient's condition improves, but the residual oedema and exudation in the trachea and bronchi may cause bronchial plug formation with subsequent death from exhaustion, obstructive atelectasis or pneumonia. The author concludes that the use of convalescent human serums, usually obtained from a member of the patient's family, is the best means of combating the infection in the respiratory passages. Humidified oxygen is very helpful in the relief of dyspnoea; repeated doses may be given if required. The intravenous administration of hypertonic human plasma often promptly reduces the subglottic oedema, with resultant improvement. The commercial dry lyophile preparation is used, but is diluted with only one-quarter of the normal volume of water employed, and an initial dose of from 25 to 40 cubic centimetres is generally sufficient. Postural drainage and foreign protein administration are also advocated.

Tuberculosis of the larynx**Treatment**

Results of X-ray therapy in unselected cases.—Engler discusses laryngeal tuberculosis and its treatment by X-rays and reports on 38 cases. For the purposes of radiotherapy he divides laryngeal tuberculosis into productive, exudative and mixed types, but his cases were unselected and he does not come to any clear conclusion with regard to the most suitable type for this treatment. Extracts from the literature show that chronic productive types of laryngitis benefit most and that acute cases of any type are unsuitable for X-ray therapy. Laryngeal tuberculosis is always secondary to pulmonary tuberculosis and is more benefited by treatment of the primary condition than by local therapy. Fractional doses give the best results and are safer than large doses. The radio-technique followed was that of Dr. Harry Hauser, head of the radiological department, Cleveland City Hospital—from 100 to 150 r every 10 days for 20 treatments, using each side of the neck for the first 10, and only one side for the second 10 treatments. The target skin distance was 50 centimetres. Using a 20 milliamperc current the output delivered was 35 r per minute. There was no instance of radio-dermatitis or skin erythema but some patients showed a mild mucous membrane reaction.

General*The pain factor*

In a Discussion on pain in laryngology Mollison stated that in some cases the site of pain may localize the lesion but that in others the pain may be referred. The V Nerve often refers pain from deep structures, for example supraorbital pain from antral infection or from acute tonsillitis. Pain near or round the ear may be referred from the sphenoidal sinus. The IX Nerve also refers pain remotely. Pain in a normal ear may be due to and be the only indication of carcinoma of the larynx. The geniculate branches of the VII Nerve may be accompanied by facial paralysis. The V and IX Nerves are responsible for neuralgias about the face, the jaws and the sinuses (Harris). Pain behind the eye may be due to irritation near the Gasserian ganglion or to oedema near the sphenopalatine ganglion. Referred earache may be associated with the glossopharyngeal nerve (Wilson). Fluoroscopic pictures of the head taken whilst the subject was eating showed in what way the condition of the teeth and disease of the temporo-mandibular joint may affect mastication and cause referred pain (Schoolman). The petrosal nerve may be the source of the deep pain behind the eye in petrositis (Fowler). The cause of the sometimes very intractable neuralgia of the gums after tooth extraction in neuropathic women was unknown. It might be due to localized periostitis (Davis). Cann remarked that pain never arose from the glossopharyngeal nerve in the throat as a result of a lesion in the ear. Again, many patients complained of a disturbance in taste after operations on the tonsils.

Baum, H. L. (1943) *Ann. Otol., etc., St. Louis*, 52, 608.

Engler, C. W. (1943) *Ann. Otol., etc., St. Louis*, 52, 655.

MacCready, P. B. (1944) *Ann. Otol., etc., St. Louis*, 53, 65.

Mollison, W. M., Harris, W., Wilson, C. P., Schoolmann, J. G., Fowler, E.

P., Jun., Davis, E. D. D., and Cann, R. J. (1944) *Proc. R. Soc. Med.*, 37, 179.

Sokolowsky, R. R. (1943) *Arch. Otolaryng., Chicago*, 38, 355.

LEPROSY

See also B.E.M.P., Vol. VII, p. 682; and Cumulative Supplement, Key No. 935.

Aetiology*The main factors*

General review of leprosy.—Frazier states that although 70 years have passed since Hansen described a bacillus as the cause of leprosy, uncertainty in its cultivation and failure to transfer the disease experimentally save in local and transitory form leaves *Mycobacterium leprae* unestablished as the cause of the disease. With the approach of aboriginal communities to

partial civilization leprosy appears in these communities and wanes as the civilization advances. The disease is endemic in India, in parts of Africa and China and in yet smaller areas of Mexico and South America. High atmospheric humidity is the only factor common to infected areas. The evidence supporting its identity with a similar disease in rats is inconclusive but coincidence in distribution of the rat flea *Xenopsylla cheopis* and of leprosy in Australia has been adduced to support the theory of an insect as the vector with rats as the reservoir of infection. What contribution hereditary transmission or predisposition makes to the familial nature of leprosy is not determined but statistics show that people exposed to household contacts run a risk of infection 5 times greater than do persons not so exposed, the risk to children being greater than that to adults. The intermixture of manifestations renders artificial the division of leprosy into nodular and anaesthetic forms. Loss of sensation to temperature, then to pain, then to touch and finally to pressure is the order of anaesthetic change; the last degree is rare. The acute and chronic exanthematous, nodular and granulomatous eruptions are very varied in form and distribution. Long periods of latency alternating with unexplained relapses give rise to scepticism about the beneficence of hydnocarpus oil and other drugs. Removal from infected areas, provision of rest and nourishment and safeguarding against injury do much to restore the patient to satisfactory life.

Causal organism

Experiments with lepromas.—Trout aseptically removed lepromas, free from secondary infection, and incubated them in sterile saline solution at 37° C. for 2 weeks or for 4 months. Cultures therefrom on egg media yielded acid-fast coccoid organisms, denominated A, in clusters surrounding rod-shaped acid-fast bacilli denominated B. By means of centrifugalizing solutions of media of various specific gravity, B was isolated and gave a greyish-white growth on subcultivation. This showed rods acid-fast after a half-minute's decolorization with acid alcohol. Both organisms form clusters which grow on all media suited to *Bacillus tuberculosis*. Both have approximately equal resistance to acid alcohol. Vaccines of A influence macular more than nodular leprosy; vaccines of B are as yet insufficiently tested. Of leprolins prepared according to Koch's old tuberculin formula and tested by intradermal, subcutaneous and scratch methods, A is inert and B seems to produce reactions. Nutrient agar 23 grammes, powdered milk 23 grammes, glycerin 40 cubic centimetres and distilled water 1,000 cubic centimetres autoclaved at 20 pounds' pressure for 15 minutes, forms a satisfactory medium.

Clinical picture

Secondary lesions

Bones.—Although the nodular and neural types of leprosy later fuse into a mixed type each has initially its characteristic bone lesion, according to Faget and Mayoral. Cooney and Crosby, whose findings largely coincide with those of the first-named workers, are less inclined to differentiate these bone lesions. Faget and Mayoral in 160 nodular cases found 9 radiographic lesions probably due to the direct action of the *Mycobacterium leprae*, namely 4 cases of enlarged nutrient canal, 3 of cyst formation and one each of necrosis and periostitis. In neural leprosy the bone changes, of which 59 examples occurred in 92 cases, resemble those of syringomyelia, tabes dorsalis and other neurotrophic diseases and are not pathognomonic of leprosy. They originate in a distant degeneration which Cooney and Crosby (citing Mitsuda and Ogawa) place in the tracts of Goll and Burdach. This leads to neurotrophic bone absorption which in the feet starts in the heads of the metatarsals or the shafts of the proximal phalanges and spreads distally. In the hands the absorption starts in the distal phalanges and spreads proximally but rarely reaches the metacarpus. Alternatively to bone absorption, and almost exclusive of each other, muscular contractures may occur, according to the involvement of trophic or of motor nerves. In both hands and feet absorption follows maximum stress and as stress is absent in contracture bone absorption is also absent. Functional activity persists in absorption but disappears in contracture. Neither calcium metabolism nor arterial circulation (the latter radiographed by injection of thorotrast during life or lipiodol at necropsy) is concerned in bone absorption; in the necrosis and enlarged nutrient canals of nodular leprosy endarteritis plays a part. Cooney and Crosby however, although they concur in the importance of stress, pressure and anaesthesia, emphasize the effect of circulatory disturbance in causing the osteosclerosis which precedes absorption. This circulatory disturbance, localized to the nutrient foramen of each bone, accounts with pressure and anaesthesia for the phenomena of concentric bone absorption.

Treatment

Curative

Trophic ulceration.—Muir records his experience of perforating ulcer of the foot in leprosy. The trophic form of ulcer differs from the other lepromatous form in the following respects: (1) in not being due to the local presence of the *Mycobacterium leprae*; (2) in being a sequel of impaired trophic and sensory supply to the foot or to the part of the foot involved; (3) in being confined to the sole of the foot whereas lepromatous ulcers are found on other parts of the foot's surface. The cause of trophic ulcer is destruction or blocking of the sensory nerves primarily by cellular pressure on and later by fibrous constriction of the axis cylinders; this deprives the foot of sensation and of trophic supply and to a certain extent involves the vascular supply; the motor nerve supply is also affected when the disease spreads to the larger mixed nerves. In the consequently impaired state a slight injury to the foot causes a perforating ulcer which may at first be superficial but is liable to septic infection. Perforating

ulcer is divided into (1) superficial and (2) deep varieties; in the latter the bones are involved and removal is essential; it is advisable to reverse the usual surgical role and to be not too conservative with regard to the amount removed. Perforating ulcer may occur in any part of the sole of the foot but by far the commonest sites are the heads of the metatarsals, the first metatarsal being the one most often involved. The author recommends a technique of metatarsectomy which he has found simple, rapid and satisfactory in its results. The wound usually takes about 3 or 4 weeks to heal but the patient should not apply the feet to the ground for another 4 weeks so as to give the fibrous tissue time to consolidate. After the first 48 hours or in simple cases in which operation is not needed the patient should be encouraged to walk about on crutches, keeping his feet carefully off the ground.

Cooney, J. P., and Crosby, E. H. (1944) *Radiology*, **42**, 14.

Faget, G. H., and Mayoral, A. (1944) *Radiology*, **42**, 1.

Frazier, C. N. (1943) *J. Amer. med. Ass.*, **123**, 466.

Muir, E. (1943) *Leprosy Rev.*, **14**, 49.

Trout, C. L. (1944) *J. trop. Med. (Hyg.)*, **47**, 1.

LEUCODERMIA

See also B.E.M.P., Vol. VII, p. 705; and Cumulative Supplement, Key No. 936.

Physiology of production of melanin

Nature and occurrence

Result of electrophoretic introduction of ferrous salts.—Rothman, Rubin and Houston report observations on the lesions of vitiligo (leucoderma), having carried out investigations on the inability of such lesions to form melanin pigment in response to pigmentogenic stimuli. The question whether or not depigmented skin in vitiligo differs in other respects from normal skin is not yet decided. The authors observed that the electrophoretic introduction of ferrous salts into normally pigmented skin caused a brown discoloration of the follicular pores. This pore pattern did not appear in depigmented skin. The local application of silver nitrate solution to pigmented skin caused a darkening of the superficial lamellae of the horny layer but no darkening was seen in the horny layer of vitiliginous areas. The reduction of the silver salt in the horny layer in pigmented skin is affected by fine melanin granules which are absent in vitiliginous lesions. It is concluded that when ferrous salts are introduced electrophoretically in vitiliginous patches the subsequent absence of a pore pattern is due to inability of the depigmented horny cells to reduce ferrous salts. Difference was not observed between the sweating function and the pilomotor response in pigmented and vitiliginous areas of skin. Hypalgesia of the vitiliginous lesions was noted in 2 out of a series of 10 patients.

Clinical picture and prognosis

Local reactions

Five cases in negro bandmen.—Freeman and Hazen describe 5 cases of vitiligo (leucoderma) of the upper lip which occurred in players of wind instruments. Each of the patients was a negro but a similar eruption has also been seen in a white man who played a trumpet. The authors cannot find any reports of similar cases in the literature. In each of the above 6 cases the mouthpiece of the instrument used was made of brass on which polish had not been used. The vitiliginous patch involved the centre of the upper lip and did not exceed $\frac{3}{4}$ -inch in diameter. There were no apparent signs of atrophy but biopsies were not made. When a patient ceased to play his instrument the lesions gradually became smaller and there was some return of pigment. There was not in any of the cases a previous history of contact dermatitis.

Freeman, C. W., and Hazen, H. H. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 605.

Rothman, S., Rubin, L., and Houston, Marietta (1943) *Arch. Derm. Syph., N.Y.*, **48**, 400.

LIPOIDOSES

See also B.E.M.P., Vol. VIII, p. 67; and Cumulative Supplement, Key Nos. 963–966.

Gaucher's disease

Morbid anatomy

The osseous type.—Later knowledge shows that the condition which Gaucher described as epithelioma of the spleen is a disordered metabolic deposit of kersin. Levine and Solis-Cohen describe 2 cases of the osseous type, without the splenic and hepatic enlargement of the commoner type. The disease is familial, congenital and predominates in females. In case (1) general radiography after a fractured humerus showed punctate osteolysis of the long bones, hands, and parieto-frontal bones. Contrary to Pick's ruling, the cortex was perforated and the periosteum invaded at the necks of the humeri. The mandible (as also in the second case) showed osteoporosis and lipid deposits around the bicuspid roots which were probably pathognomonic. The characteristic Erlenmeyer flask appearance at the lower end of the femur, which afforded diagnosis in case (2), was absent. As all the other systems were normal and laboratory investigations uninformative, bone biopsy was necessary in order to exclude xanthomatosis, multiple myelomas and sarcomas and osteitis fibrosa cystica. The marrow showed Gaucher cells, polygonal, hyaline, measuring 20 to 80 μ and usually mononuclear.

After fixation with picric acid and ammonium bichromate, the kersin stains light blue with Mallory's stain and acid fuchsin. Case (2) illustrates the value of splenectomy in abolishing haemorrhages due to thrombocytopenia and the intractability of the sinuses which persisted after erroneous exploration for osteomyelitis.

Niemann-Pick disease

Clinical picture

Report of a case in infancy.—Canmann records a case displaying the syndrome of xanthomatosis, phosphatide lipoidosis and lipid splenomegaly which is usually called Niemann-Pick disease. Since Niemann in 1914 described 'an unknown disease picture', 62 cases have been recorded. The phenomena include a yellow skin, a Mongolian appearance, emaciation and enlarged liver and spleen, with oedema and often ascites. The disease is probably congenital, predominantly affects the Jewish race, is familial in some 30 per cent of cases and is always fatal by the thirtieth month. The patient described, a girl aged 10 weeks, illustrates the characteristic symptoms and post-mortem findings. She was however of Gentile stock and her only sibling was healthy. She was admitted to hospital with constipation, cyanosis, oedematous feet, vomiting and emaciation. The liver was much enlarged. Her mother reported one yellow stool every 3 days attained by glycerin suppository, and a gain of one ounce in weight only since birth. The erythrocyte count was 4,050,000 per cubic millimetre (13 per cent of the erythrocytes were nucleated) and the leucocyte count was 20,400 with 30 per cent of vacuolated lymphocytes. Death ensued 30 hours after admission. Necropsy showed heart, lungs, liver and spleen to be greatly over the normal weight. The liver was yellow with purple patches and was disorganized. Microscopically the cells, which were oval, not polygonal, were filled with fatty globules and foamy material which showed best with Mallory's stain. The bone marrow was almost equally disorganized and in lesser degree foam cells pervaded the lungs, pancreas, spleen and thymus gland. In a discussion of the differential diagnosis of the condition, it is mentioned that a red spot in the macula is often seen, as in Tay-Sachs's disease, which disease is however confined to the nervous system. The other possible confusion is with Gaucher's disease.

Canmann, M. F. (1944) *J. Pediat.*, **24**, 335.

Levine, S., and Solis-Cohen, L. (1943) *Amer. J. Roentgenol.*, **50**, 765.

LIVER DISEASES: LIVER FUNCTION TESTS

See also B.E.M.P., Vol. VIII, p. 81; and Cumulative Supplement, Key No. 967.

Scope and significance

Serum protein changes in hepatic disease

Post and Patek review the serum protein changes in liver disorders. The serum proteins are in a constant dynamic state. Albumin appears to be formed in the liver, and there is evidence to suggest that globulin originates in the reticulo-endothelial cells; fibrinogen and prothrombin are probably formed in the liver. In acute hepatitis only moderate alteration of the serum proteins occurs but in acute or subacute yellow atrophy and in cirrhosis serum albumin is reduced. Acute hepatitis affects the prothrombin level however and vitamin K administration is ineffective in cases of severe liver damage. Serum globulin shows an elevation in chronic liver disease, and the albumin content can be used as a prognostic index; in those patients who improve and remain in good health for indefinite periods of time the serum albumin rises to normal levels and remains within that range, whereas in those in whom the course is unfavourable the serum albumin either remains low or declines. The relation of the serum protein level to transudation of oedema fluid is seen in nephrotic syndromes, in protein starvation and in ascites. The authors consider that reduced serum albumin is an essential factor in the ascites of liver disease whereas the portal hypertension merely determines the site at which the transfer of fluid takes place. When ascites occurs in the presence of normal serum albumin it is an indication that an extrahepatic cause should be sought. The actual mechanism of serum albumin reduction may arise from protein starvation, excessive utilization or impaired synthesis. Protein starvation reduces the albumin blood content but there is not elevation of the serum globulin. Nitrogen balance studies have shown that patients with cirrhosis of the liver can absorb and retain protein but that there is an apparent defect in the synthesis of serum albumin.

Investigations with 5 tests

Critical survey in various diseases.—Higgins, O'Brien, Stewart and Witts emphasize the fact that tests of hepatic function should conform to 3 conditions. First, they must be applied to many healthy controls for the purpose of determining the limits of normal variation. Secondly, the hepatic diseases in which the tests are made must be of assured diagnosis. Thirdly, in order to ensure that such tests are pathognomonic of hepatic disease they must be proved negative in all possible extraneous diseases. The tests propounded by the authors are the estimations of (1) plasma bilirubin, (2) phosphatase, (3) proteins, (4) hippuric acid excretion and (5) modified laevulose tolerance. The hepatic diseases investigated comprised secondary carcinoma and acute, subacute and chronic hepatitis or cirrhosis; the cases totalled 71. A group of 100 healthy individuals provided the normal limits and miscellaneous diseases were represented by 62 cases. All tests gave readings which differed significantly from the normal and from those of extraneous diseases. As tests of function and criteria of hepatic damage

the tests were found to possess prognostic value but their value in differential diagnosis of hepatic disease was limited. The finding of plasma bilirubin was a prognostic guide in acute hepatitis only. The degree of rise in plasma phosphatase and of fall in hippuric acid excretion were not closely correlated to clinical conditions and the evidence they afforded of liver damage was corroborative only. Plasma protein, little disturbed in acute hepatitis, was deeply significant when found in subacute and chronic hepatitis. Readings below 3.5 grammes per cent indicated a poor margin of reserve and, especially, a preponderance of globulin in the albumin-globulin ratio indicated irreparable damage. The laevulose index, in subacute and chronic hepatitis only, was a reliable criterion of liver damage although it was inconvenient in use since it required repeated venepuncture, whereas one specimen sufficed for the other tests. The authors found that more diagnostic and prognostic information could be obtained from the results of the 5 tests when they were applied to the same individual than could be obtained from the result of any one test.

Tests

Intravenous hippuric acid

Its use in infective diseases of children.—Meneghello and Drinberg have used the intravenous hippuric acid test in the investigation of hepatic function in 128 children with infective diseases. Sixteen healthy controls were tested and the minimum normal hippuric acid excretion was thus established. The dose given was 2 grammes of sodium benzoate in 20 cubic centimetres of water. The test gave normal results in whooping-cough, typhus fever and acute upper respiratory infections. Impaired excretion was observed in 80 per cent of children with scarlet fever, 91 per cent of those with diphtheria, 27 per cent of those with typhoid fever and in all patients with lobar pneumonia and tuberculous meningitis.

Higgins, G., O'Brien, J. R. P., Stewart, Alice, and Witts, L. J. (1944) *Brit. med. J.*, **1**, 211.

Meneghello, J., and Drinberg, M. (1943) *Amer. J. Dis. Child.*, **66**, 103.

Post, J., and Patek, A. J., Jun. (1943) *Bull. N.Y. Acad. Med.*, **19**, 815.

LIVER DISEASES: HEPATITIS, ACUTE AND SUBACUTE

See also B.E.M.P., Vol. VIII, p. 104; and Cumulative Supplement, Key No. 973.

Clinical and aetiological types

Catarrhal jaundice (infective hepatitis)

Course and prognosis.—Infective hepatitis was discussed by Lisney, Ford, Davis and Spooner at a meeting of the epidemiological section of the Royal Society of Medicine. All agreed that it is a disease of the winter months, and mainly affects children between the ages of 5 and 15 years. It was however also prevalent amongst European troops in the campaign in the North African desert. It is endemic in certain localities in Great Britain, such as the Isle of Dogs and Wembley. Hirsch states that epidemic icterus was first reported in 1745 from Minorca. It is differentiated from Weil's spirochaetal jaundice by animal inoculation of a centrifuged deposit of blood or urine. All attempts to isolate a causative organism have failed, and there is no evidence that the disease is spread by milk, water, food or vermin; spread appears to be from patient to patient by direct contact. Mild or abortive cases without jaundice or changes in the stools and urine are common; these lead to difficulty in tracing infection. The infective period lasts for about a week, and ends with the appearance of the jaundice; the incubation period is approximately one month. The typical blood picture is a monocytosis varying from 2 to 19 per cent. Clinically there is a prodromal period of several days with headache, anorexia and bradycardia, after which pain in the upper abdomen, epigastric tenderness, enlargement of the liver, often vomiting, and jaundice with bile in the urine occur. The main complication is pancreatitis. Recovery is sometimes very slow, especially in adults, but the death rate is low. There is no specific treatment.

Problems of infective hepatitis.—Witts discusses some problematical aspects of infective hepatitis. Although a virus has been considered to be the cause such a virus has never been demonstrated and has never been transmitted to experimental animals. Post-arsenical jaundice and homologous serum jaundice have a longer incubation period (60–90 days), do not appear to be infectious, and whereas an attack of infective hepatitis appears to produce immunity to further infection, homologous serum jaundice increases the susceptibility to the infective disease. Difficulties in diagnosis of infective hepatitis in the pre-icteric stage are great and malaria especially presents the greatest difficulty; it is wise to treat the case as malaria unless subsequently disproved. There is a suspicion that the virus may at times attack the nervous system. Since the mortality rate is less than 1 in 1,000, it is difficult to prove the value of any specific treatment. A study of possible predisposing factors fails to reveal any obvious incriminating cause. Epidemiological study is rendered inaccurate by the movements of troops and their losses and replacements and because figures collected over several months may represent not a continuous epidemic but an aggregate of a number of minor epidemics. In studying the latter a pattern evidently evolves. A herald case occurs, then perhaps another after an interval of from 1 to 3 weeks; a similar interval occurs and then comes the epidemic. The incidence of jaundice in Africa among the troops was high and the disease is endemic throughout the whole Mediterranean area. British Army officers were affected four times more frequently than were other ranks and evidence is presented which appears to incriminate

unsatisfactorily washed crockery as a source of infection; no definite conclusion however is arrived at. Further investigation is required in order to ascertain the influence of insects and of excreta in the dissemination of the disease.

Jaundice due to other drugs and chemical poisons

Toxicopathic and trophopathic hepatitis.—Cirrhosis of the liver has been experimentally produced by the giving of abnormal diets, and in some animals taking such diets hepatic necrosis occasionally develops. It was assumed that this necrosis was but a transient stage in the sequence leading to cirrhosis but Himsworth and Glynn state that the two conditions are entirely distinct. They distinguish two types of experimental hepatitis in rats. They propose the term, toxicopathic hepatitis, for the hepatitis due to the direct action of noxious substances on liver cells and the term, trophopathic hepatitis, for that due to dietary deficiency of a component of protein. Toxicopathic hepatitis develops rapidly after the subject has been exposed to the poison. The liver shows a diffuse zonal necrosis. In survivors recovery is complete. Repeated exposures to the poison produce a diffuse hepatic fibrosis. Trophopathic hepatitis develops slowly. The liver shows massive necrosis which always leads to post-necrotic scarring and in severe cases to nodular hyperplasia. In man the hepatitis which develops after exposure to such poisons as chloroform, phosphorus and carbon tetrachloride has features of a toxicopathic hepatitis, and so has the zonal hepatitis which is seen in eclampsia and in infective hepatitis and after treatment with organic arsenical preparations. Association of two or more weak toxicopathic agents may produce a great incidence of severe hepatitis. In man, massive hepatic necrosis and its sequel nodular hyperplasia may be attributed to a trophopathic hepatitis. There is evidence that this can arise as the direct result of a dietary deficiency. Usually however it develops as a complication of a preceding illness and should then be regarded as a conditioned deficiency disease separate from the illness which it complicates. Restriction of the intrahepatic circulation is an important predisposing cause of trophopathic hepatitis in man. It usually results from the swelling of liver cells which have been previously injured by a toxicopathic agent. Pregnancy, vomiting and anorexia contribute to the development of a trophopathic hepatitis by reducing the amount of protective nutriment available to the liver cells. An increased metabolic rate may act in the same way by increasing the general bodily needs for protein. It is also possible that certain poisons such as selenium and trinitrotoluene can produce the condition by so combining with components of protein as to render them useless.

Himsworth, H. P., and Glynn, L. E. (1944) *Lancet*, **1**, 457.

Lisney, A. A., Ford, J. C., Davis, E., and Spooner, E. T. C. (1944) *Proc. R. Soc. Med.*, **37**, 165.

Witts, L. J. (1944) *Brit. med. J.*, **1**, 739.

LIVER DISEASES: HEPATITIS, CHRONIC

See also B.E.M.P., Vol. VIII, p. 118; and Cumulative Supplement, Key No. 974.

Morbid anatomy and pathogeny

Liver

Cirrhosis defined and reviewed.—Karsner says that the term, cirrhosis, should be applied only to the liver; it is not synonymous with fibrosis or gliosis. He mentions the triad found in cirrhosis: proliferation of connective tissue, degeneration and death of hepatic cells. In this can be included the Laennec type, fatty cirrhosis, haemochromatotic cirrhosis and biliary cirrhosis. Since cirrhosis is a form of chronic inflammation, carcinoma may ensue. Juvenile cirrhosis may be due to congenital syphilis, to atresia or malformation of bile ducts, to infectious disease or to unknown factors. Erythroblastosis foetalis may be related to cirrhosis. At the age of 50 years the incidence of cirrhosis is greatest. It is more often found in males than in females. Congestive cirrhosis may occur with hypertensive heart disease. Post-necrotic cirrhosis is found more often in women as a sequel to acute yellow atrophy or to infective diseases. Hanot's cirrhosis may be either intrahepatic cholangitic or cholangiolitic cirrhosis. Intrahepatic cholangitic biliary cirrhosis is a rare form of the disease. Obstructive biliary cirrhosis resembles Laennec's cirrhosis with bile pigmentation. This form has been found in children as well as in adults. Pigmentary cirrhosis (haemochromatosis) may be due to injury of the cells resulting in acute hepatitis with disturbance of iron metabolism. Fatty cirrhosis is Laennec's cirrhosis with infiltration of fat into the parenchyma. There may be 3 stages: (1) acute fatty liver due to alcoholism; (2) early progressive fibrosis; (3) nodular cirrhosis with shrinkage. In Banti's syndrome there are no morphological changes in either the liver or spleen which would make this disease an anatomical entity. Wilson's disease is a combination of lenticular degeneration and hepatic cirrhosis. Laennec's cirrhosis is the small nodular form of the disease which has been called atrophic cirrhosis. It may be divided into an active and a latent or healed stage. The signs of activity include degenerated parenchyma, fibroblastic proliferation and infiltration of mononuclear and polymorphonuclear cells. The latent stage shows absence of degeneration, of hyaline droplets or of infiltration of polymorphonuclear leucocytes.

Prognosis

Chronic hepatitis in children

Preponderance of progressive cirrhosis.—Amberg discusses the prognosis in chronic hepatitis

in children, and points out that comprehensive observations on the duration of the disease in children do not appear to have been published. The author has studied 69 cases. At present there are not any criteria by which to identify different types of chronic juvenile hepatitis which either heal completely or result in a damaged but still functioning organ. Most of the cases encountered were of progressive cirrhosis with parenchymatous degeneration which was ultimately fatal. The actual duration of the disease could not always be determined accurately, but was less than 2 years in 13 cases, from 2 to 4 years in 12 cases, and 5 years or longer in 8 cases. In 2 instances the patients lived about 10 years after splenectomy. In several cases a diagnosis of Banti's disease had been made, but clinical and microscopical evidence does not suggest that Banti's disease should be regarded as a special syndrome, and splenectomy is not always curative. In 5 cases the hepatitis appeared to be secondary to chronic ulcerative colitis; in 2 instances the hepatitis seems to be healing, but the duration of the condition is still short. In catarrhal jaundice (epidemic or sporadic hepatitis) the course is usually short with ultimate recovery, but in some patients acute fatal yellow atrophy develops which is of a more protracted type of hepatitis with periodic exacerbations. Three cases of sub-chronic hepatitis (yellow atrophy of Seyfarth) are reported on.

Amberg, S. (1943) *Proc. Mayo Clin.*, **18**, 494.

Karsner, H. T. (1943) *Amer. J. clin. Path.*, **13**, 569.

LUNG DISEASES: ABSCESS AND GANGRENE

See also B.E.M.P., Vol. VIII, p. 172; and Cumulative Supplement, Key No. 987.

Clinical picture

Single abscess

Review of surgical features.—The surgical section (Sellors) of a composite paper deals preponderantly with the solitary putrid abscess of the lung which is caused by pyogenic organisms. The situation of the abscess is usually peripheral with pleural adhesions and, owing to the anatomical dispositions of the bronchial branches, the most common sites are the posterior upper lobe and the apex of the lower lobe. The danger of conservative postural treatment is chronic deterioration with permanent secondary lung damage which can be only incompletely benefited by subsequent surgical treatment. Neuhoof's early one-stage drainage while the pleural adhesions are firm is advocated—thus avoiding opening of the pleural cavity as in the 2-stage method in which actual drainage is postponed for 10–14 days—and, if the pleura appears to be free, an iodine pack is inserted and the wound is closed for 2 weeks. As radiology alone cannot give the complete diagnosis, the importance of interpretation of X-ray films in association with the clinical picture is stressed. Postero-anterior and lateral views should always be taken and the use of the aspirating needle avoided. Blair, in the section on radiology, states that the cavity of the acute localized pyogenic lung abscess usually contains a fluid level and a central slough; it is situated peripherally with surrounding reaction or consolidation which gives place quite suddenly to normal living structure but without a completely clear-cut, well defined border except where it presents on a pleural surface. The opacity is at first confined to a bronchial segment but it later spreads and is not strictly segmental. The relation of the shadow to the lung fissures is an important diagnostic point. In the differential diagnosis of shadows resembling lung abscesses, shadows due to disintegration of lung tissue from other causes are especially mentioned. In the medical section Houghton discusses the aetiology, clinical course and complications of lung abscesses. In most cases there is no specific causative factor or bacteriology, but as a general rule the putrid type of lung abscess is associated with anaerobic and the non-putrid with aerobic organisms. The identification of the type of organisms is important as it influences the course of the illness and the mode of treatment. Unless the organism can be demonstrated predominantly or in almost pure culture the sulphonamides do not seem to be effective. Evaluation of medical treatment is difficult and non-surgical cases are best treated on the same lines as general sanatorium treatment of pulmonary tuberculosis.

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LUNG DISEASES: TUBERCULOSIS

See also B.E.M.P., Vol. VIII, p. 182; Interim Supplement, No. 16*; and Cumulative Supplement, Key No. 988.

Aetiology

Climate

Investigations of effects of meteorological environment.—Howe and Mayne consider the influence of environmental factors on fever in pulmonary tuberculosis. Clinicians have noted tendencies for the entire population of a sanatorium to show parallel movements in temperature from day to day. Patients were studied for 14 months at a sanatorium in Illinois. The number of patients ranged from 68 to 96. Daily temperature readings were taken at 8 a.m., 4 p.m. and 8 p.m. Patients whose temperature was 99° F. or higher at any one daily reading were considered to be febrile. The authors investigated the effects of the meteorological

environment, and admittedly assume that the population of a sanatorium is homogeneous from week to week with respect to the tendency to be febrile under similar conditions for the period of observation. The percentage of febrile patients rises rapidly from early April to reach in late May a peak which is maintained until early July. The curve then falls rapidly until late August when there is a sharp secondary rise which continues into September, followed by a second fall and another rise which persists through October. The spring activation of tuberculosis has been noted from the time of Hippocrates. If the mean environmental temperature is compared, there is a roughly similar trend. It seems that the seasonal trend of fever in tuberculous patients is not a simple effect of higher environmental temperature. There is a weekly cycle of temperature rises with Wednesday and Sunday as the peak days. It is possible that the cycle is associated with underlying short cycles in the weather, but the more likely explanation is that the weekly variations were associated with the visiting days. A clear relation was seen between atmospheric temperature and day-to-day changes in the percentage of febrile patients. This relation was most noticeable in summer when the patients were more directly exposed to changes in atmospheric temperature. Such changes may be due to the lability of the heat regulating mechanisms in tuberculous patients.

Tuberculosis in young children

Danger of the adult carrier.—Fleming discusses pulmonary tuberculosis in children, and points out that in fatal cases a large majority of patients are infected from a human source and through the respiratory tract. The younger the age at which infection takes place the greater the risk to life. These facts are concealed in our statistics because deaths from tuberculous meningitis are included in the non-pulmonary group, although in a large number of these cases the primary focus is in the lung. From the records of some 350 fatal cases of tuberculosis at the Royal Hospital for Sick Children, Glasgow, the usual fatal termination was shown as tuberculous meningitis which often developed in the patient before chest signs became evident, but the primary focus was found in the lungs in from 74 to 80 per cent of the cases. Infection under the age of 4 years is particularly dangerous; one-third of the number of those children admitted to the Royal Hospital with a positive Mantoux reaction died of meningitis. The obvious lesson to be drawn is that children under 4 years of age must be shielded from human infection by isolating adult carriers from contact with them. The young child with early infection, on the other hand, does not require isolation but should live in good conditions in the country with an ample supply of milk, cod-liver oil and vitamin D.

Statistics of incidence at the tuberculosis colony at Papworth.—Statistics of the incidence of infection among the children at the Papworth Tuberculosis Colony, England, are presented by Brieger. During the 20 years ending 1938, 199 ex-patients' families occupied cottages in the village. Of these families 137 included children. The period of residence ranged from under 5 to 20 years. In 57 families the head of the family was persistently sputum-positive; in 63, 'sputum-converted'. Children born in the village numbered 108. Of these children none have died from tuberculosis; 4 were still-born and 2 have died from other causes. No clinical or radiological evidence of active tuberculosis anywhere in the body has been observed in any of these children. In regard to latent lesions, 51 per cent did not have any clinical or radiological findings; 42.5 per cent had radiological evidence of calcified foci not exceeding those observed in any mixed child population; 4.6 per cent showed radiological evidence of an abortive primary lung lesion and 1.8 of a transient perifocal reaction. The 2 children included under the last heading were both offspring of sputum-positive parents. Of the 5 cases of residual pulmonary infiltration, 3 occurred in the families of healthy employees, one in the family of a sputum-positive patient and one in the family of a patient with surgical tuberculosis. Among the children admitted to the colony, the children of healthy employees have shown the same low incidence as children born in the village, and the children of sputum-negative and surgical patients an incidence almost as low. The children of sputum-positive patients show a high degree of infection acquired prior to admission. On the other hand, none of the active childhood type of lesions have developed during the stay at Papworth.

Course and prognosis

Bronchiectasis and pulmonary tuberculosis

Lipiodol method of radiography.—Tuberculous bronchiectasis usually may be unimportant but Rilance and Gerstl analyse 47 cases illustrating its occasional malevolence. The lipiodol method of study was used in 35 instances. In 3 patients the association seemed to be accidental, the tuberculosis being apical and the bronchiectasis basal. Of 22 patients with bacilli in the sputum, in 17 the sputum became negative and radiography showed amelioration yet the physical signs of active tuberculosis persisted. In 5 the sputum remained positive although radiography proved amelioration. In 10 patients physical signs and symptoms indicated acute tuberculosis yet the sputum remained negative throughout and radiography showed fibroid tuberculosis. In 12 necropsies 3 non-tuberculous abscesses occurred, one cerebral, one hepatic and one renal. Suppuration distal to a bronchostenosis caused the death of 2 patients. Bronchiectasis here appears responsible, first for persisting physical signs after activity has ceased, secondly for persistence of tubercle bacilli in the sputum although lesions were healing and thirdly for suppurations shown at necropsy. Four cases illustrated a positive sputum which persisted for more than 4 years in improving patients. A fifth case illustrated the patient's dramatic response to sulphathiazole. Radiography with lipiodol showed coincidence of the major areas of tuberculosis and bronchiectasis in 25 cases. They did not coincide in 7. The

propinquity of fibrosis and bronchiectasis in the non-tuberculous form is absent in the tuberculous, which is characterized by grosser distortion and angularity of the bronchial tree. Whereas contraction of fibrous tissue explains the non-tuberculous form here some pathological process acts, perhaps occlusion of the bronchial arteries or erosion of the bronchial walls by pyogenic organisms.

Diagnosis and differential diagnosis

X-rays

Mass radiography in diagnosis.—Trail reviews the new approach to the diagnosis of pulmonary tuberculosis by means of mass radiography. The necessity for early diagnosis of the disease has two aspects, the national and the individual. Direct loss to national economy through pulmonary tuberculosis is incalculable. Every sufferer before his return to work or before death from the disease involves expenditure varying from £200 to £1,000, and in many cases this outlay is not of any avail. Pulmonary tuberculosis causes half the number of total deaths from natural causes between the ages of 15 and 24 years, an age group of most importance to the community. From the individual aspect the outlook for patients treated by the best available methods depends upon the extent of the disease when it is diagnosed. The 5-year survival rate after diagnosis is not very heartening; for early cases it is over 80 per cent, but for moderate or advanced cases it decreases from 40 to 8 per cent. Unfortunately few patients have any dramatic warning from symptoms in the early stages and there is not any fixed correlation between the extent of the disease and the illness produced. The great majority of patients already have fairly advanced lesions when first examined. Mass X-ray investigation is particularly valuable, since it seeks out those who need immediate advice and possibly treatment and demonstrates pulmonary tuberculosis even before there are positive physical signs. Much education of the public, however, is still necessary before it is generally accepted that this mode of investigation is of value to the individual who can take advantage of it. Unfortunately scarcity of apparatus and of trained staff will be a hindrance for some considerable time; meanwhile educative propaganda should urge a more general use of this new and powerful weapon against the scourge of tuberculosis.

Routine examinations confirmed by bacteriological examination.—A report on bacteriological examination supplementary to routine radiography in the Australian military forces is published by Webster. The value of such examinations as a check on the radiological diagnosis of pulmonary tuberculosis is emphasized. The specimens were secured in the early morning after a night's fast. If the recruit was unable to produce a satisfactory specimen of sputum a sample of stomach contents was obtained by means of a Rehfuess tube. Direct microscopy was performed and if it was negative cultures were made. Acid-fast bacilli demonstrated by either method in the sputum of people whose pulmonary lesions were assessed radiologically as active were accepted as tubercle bacilli. Any acid-fast bacillus cultivated from the sputum of people with radiological evidence of healed, inactive or doubtful tuberculosis and any demonstrated in the gastric mucus were tested for virulence in the guinea-pig. The total number of bacteriological examinations carried out on recruits suspected on radiological grounds of pulmonary tuberculosis was 1,548; 364 of them were shown to be discharging tubercle bacilli. In 192 of these the bacilli were demonstrated in the gastric contents. Bacteriological confirmation of the X-ray findings was obtained in 53·8 per cent of cases classified as active. In 14·3 per cent of those classified as doubtfully active, in 5·6 per cent of those classified as healed or inactive and in 9·3 per cent of those classified as doubtfully tuberculous, positive results were obtained, a fact which provides a strong argument for confirmatory bacteriological examination in all such cases.

In selection of American army recruits.—Long and Stearns of the Army of the United States describe the radiological standards required in the chest films of men drafted for the American Army. In 1940 the broad principle was adopted that the chests of all recruits were to be radiographed and all men showing active tuberculosis excluded. As the speed of mobilization increased, it was found necessary to lay down definite limits regarding the character and extent of the shadows of inactive and healed lesions permissible in men accepted for service. Stereoscopic 4×5-inch roentgenograms of the chest are projected to 14×17-inch screen pictures. Calcified residues of lesions of the intrathoracic lymphatic glands were declared to be admissible provided none exceeded 1·5 centimetres in diameter in the screen picture and the total number did not exceed 5, and also calcified parenchymatous lesions up to a limit of 10, one of which might equal but not exceed a diameter of 1 centimetre provided none of the remainder exceeded 0·5 centimetre. The shadows should be isolated, sharply circumscribed, homogeneous and dense. It was found that insistence on these measurements excluded a number of men who were perfectly healthy. In October 1942 a qualifying paragraph was added, enabling further consideration to be given to persons with calcified lesions exceeding these limits in number and size, if the state of the individual's health warranted the opinion that the lesions were healed.

Existence of unsuspected pulmonary disease.—Childress, Debbie and Harmon report the results of routine X-ray chest examinations made on 7,187 individuals treated at Grasslands Hospital, Westchester, N.Y., during a period of 18 months from July 1941 to January 1943. These patients were not suspected of having pulmonary disease and ordinarily would not have been examined in this way. The out-patients, who numbered 2,471, were screened and the 4,716 in-patients had films 14×17 inches taken. It was found that the proportion of active or

questionably active cases was practically identical in both groups. Those patients found to be suspicious on screening had films taken later. Approximately 4 per cent of those examined showed evidence of tuberculosis infection; 0.6 per cent had active or questionably active disease requiring hospital treatment or close observation. Activity was later established in 0.35 per cent. Of these the larger number were men over 30 years of age. The observers point out that hospital X-ray equipment can be used for routine screening of chests with a minimum of dislocation of material and staff, and that routine examination of all hospital patients would bring to light a large number of unsuspected sources of infection.

Detection of tuberculosis in mental patients.—Snell, MacMahon and Heaf report the results of an investigation into the incidence of pulmonary tuberculosis in a mental hospital. Preliminary radiological examination was carried out in all cases, miniature films being used for 2,035 patients and 224 staff and full-sized films for 231 patients of whom 183 were bedridden, deformed or resistant and 48 had already been notified as cases of pulmonary tuberculosis. In any case in which the miniature films were suspicious full-sized radiographs were taken, and all suspects were subjected to clinical and pathological examination. The survey resulted in the detection of 36 new cases of active pulmonary tuberculosis among the patients, none in the staff. Inactive lesions were discovered in 87. Of the patients previously notified as tuberculous 19 gave negative X-rays. The patients were chiefly those with some congenital mental defect. An acute type of pulmonary tuberculosis appears to be common among such patients. Fifteen have died of the disease in the 8 months since the survey was undertaken, and of these 6 gave negative X-rays at the time. The authors consider that for mental patients the routine use of 15 × 12-inch films is preferable to miniature radiography.

Tuberculosis control.—Hilleboe of the Tuberculosis Control Section, Division of State Relations, Washington, read a paper at the Meeting of the American Roentgen Ray Society at Chicago in September 1942 on the tuberculosis control programme of the United States Public Health Service. In order to prevent an increase in tuberculosis on account of the war, the U.S. Public Health Service had set up an office of Tuberculosis Control at Washington. Their practical objectives were (1) widespread chest X-ray examinations of workers in war industries and of their families, especially those belonging to minority and under-privileged groups; (2) extension of the Army and Navy X-ray examinations to coast-guard recruits, and notification to their local health departments of all recruits rejected because of tuberculosis; (3) the provision of a tuberculosis consultation service to organize State control programmes on a war-time basis. Eight miniature X-ray units, consisting of a medical officer, technician, clerk and full equipment for taking 35-millimetre films, have been formed and are lent to State health departments for limited periods on request. With good cooperation and team work, from 300 to 500 workers can be examined in a day. Experience has shown that less than 10 per cent of minimal lesions are missed. Of these minimal cases, one-third have proved to be clinically inactive, and another third are questionably tuberculous.

Fluorography

Brooks, after stressing the importance of early diagnosis of pulmonary tuberculosis, quotes from the notification statistics of the London County Council to show that without the aid of fluorography only 20 per cent of the cases notified in the years 1927–37 were in the classification groups A and B, (sputum – and early sputum + cases), and that even of this 20 per cent many were relatively advanced cases no longer to be regarded as ‘minimal pulmonary tuberculosis’. Fluorographic investigation applied to 479,373 apparently healthy men of the Royal Navy, and to 23,344 members of the Women’s Royal Naval Service disclosed radiological evidence of disease in 6,077 (1.2 per cent) and 213 (0.91 per cent) respectively. Of the male group, full in-patient hospital investigation was applied to 2,911, from which it appeared that in 21 per cent the lesion could be regarded as healed, in 63 per cent as apparently but not certainly inactive and in 16 per cent as definitely active and progressive. In the case of W.R.N.S. the active percentage was 18. On the basis of this large yield of suspected and active ‘minimal tuberculosis’ in a selected presumably healthy population group, questions arise which relate to the even larger numbers likely to be disclosed in industrial and other civil groups and to the steps it is necessary to take in order to enable such numbers to receive benefit from early detection of the disease. It is emphasized that full investigation in hospital is essential for the purpose of deciding which of these cases are active and require full and prompt treatment by collapse therapy, in sanatoria and so forth and which can be regarded as of unproven activity. In the latter event the patients should be kept under observation for 2 years with bi-annual radiographical check and the working and environmental conditions should be modified according to the circumstances of each case.

Tuberculin patch test

Grozin’s modification.—The tuberculin patch test has the disadvantage that the area of reaction remains concealed so that the successive phases cannot be followed. To overcome this drawback Grozin has devised the following method. A strip of adhesive plaster 1½ inches wide and 3½ inches long is placed sticky side downwards. In the centre of each third of the strip a hinged flap is made by cutting an incomplete circle. The non-sticky surface of another strip of plaster is moistened with tuberculin and cut into ½ inch squares, one of which is laid on the first and third of the hinged flaps in such a way that the non-sticky side is in contact with the skin when the ‘lid’ is closed. On the middle flap is laid a similar square of

untreated strapping as a control. The strapping is now applied to the skin. The lids can be opened at intervals for inspection.

Stomach lavage

Value in cases in which a positive sputum is unobtainable.—Foley and Andosca stress the value of the examination of gastric contents for tubercle bacilli in cases of suspected pulmonary tuberculosis with negative sputum examinations and they describe the technique employed. In 639 sputum-negative cases 187, or 29·2 per cent, showed tubercle bacilli by gastric lavage whereas 32 non-tuberculous cases gave negative results. A Levine tube is passed through the nose into the stomach in the early morning before the ingestion of food and with a Luer syringe 30-50 cubic centimetres of stomach contents are aspirated. The specimen is digested in a 1 per cent solution of sodium hydroxide containing 0·2 per cent potassium alum and ·002 per cent bromthymol blue in a water bath at 37° C. for 30 minutes with occasional shaking. Then 2·5 normal hydrochloric acid is added drop by drop with shaking until the colour indicator denotes approximate neutrality. Shake for 30 seconds and if flocculation does not occur add 0·2 cubic centimetre ferric chloride solution and shake again. Centrifuge the flocculated sample for 5 minutes at top speed, discard supernatant fluid, prepare uniform smears on slides, dry in air, fix by heat and stain by the Ziehl-Neelsen method. Thorough cleaning of the stomach tubes is essential to prevent false positive reports.

Treatment

Cure

Tubercle endotoxoid.—Grasset reports on tubercle endotoxoid in the treatment of tuberculosis among South African natives. This group constitutes a stock which has only recently come in contact with the disease, amongst whom it accordingly runs a natural course. The dose ranged from 0·1 cubic centimetre to 2 cubic centimetres. Reactions were of a mild nature. The final dose of 2 cubic centimetres was given twice a week for several months. Stabilization and then gain of weight, diminution of night sweats and abatement of cough were among the general signs of improvement. Fall in temperature and reduction of pulse and respiration rates were other features. In many cases X-ray examination showed appreciable changes after only 3 or 4 months with localized exudative lesions resolved by a fibrotic process. In cases of extensive involvement transformation into the chronic fibrocaseous or fibrotic type of the adult European was seen. Artificial pneumothorax was combined in some cases with endotoxoid treatment and proved to be beneficial. Histological examination of post-mortem material confirmed the healing nature of the clinical and radiological changes which were observed; lymph glands showed similar changes. Extrapulmonary forms of tuberculosis in natives were also improved by endotoxin injections. Grasset emphasizes that the results are of special significance since the acute uncomplicated course of the infection in these subjects approximates to those of experimentation, whereas in assessing results in Europeans the factors of individual immunity and resistance are sources of difficulty. By contrast the majority of South African natives constitute 'virgin soil' for tuberculous infection. The specificity of endotoxin is evidenced by its therapeutic action on tuberculous conditions irrespective of the involved site. In a previous paper the author reported the finding of specific anti-endotoxigenic tuberculosis antibodies in the blood of horses which were submitted to a course of increasing doses of tubercle endotoxoid.

Experiments with four new sulphone derivatives.—Smith, Emmart and Stohlman continue investigations into the chemotherapy of tuberculosis with 4 new derivatives of the sulphone series. It has been shown that 4 : 4'-diaminodiphenylsulphone (diaminosulphone) is the most effective of these agents in inhibiting the growth of the tubercle bacillus *in vitro*, but its excessive toxicity rendered it unusable in man. Fortunately the guinea-pig in addition to maintaining a uniform response to experimental infection with tuberculosis tolerates, weight for weight, much heavier doses of this drug and of its less toxic sulphonated dextrose derivative, promin, than does man. Using promin as their standard these investigators estimated the toxicity, dosage, blood levels and therapeutic effectiveness of 4 new derivatives of 4 : 4'-diaminodiphenylsulphone in the guinea-pig, also their inhibiting action towards growth of the tubercle bacillus *in vitro*. The results of the experiments go to show that the beneficial effects of this type of drug are due possibly to an attenuating action on the bacillus, and that the N-phosphoryl derivative of diaminodiphenylsulphone has advantages over promin, which in turn is superior to the nitro, hydroxy, and sodium formaldehyde sulphonylate derivatives.

Diasone.—Petter and Prenzlau report on a clinical investigation of the treatment of tuberculosis with the disodium formaldehyde sulphonylate derivative of 4 : 4'-diaminodiphenylsulphone. This compound (called diasone) was synthesized in 1938 by Raiziss and his associates and was shown to be less toxic than the sulphonamides. A few patients were first selected for diasone treatment because they had infiltrative lesions, without cavitation, theoretically similar to those of guinea-pig tuberculosis. Favourable changes were noted after 60 days of therapy. Accordingly, 100 patients, representing a cross-section of the sanatorium population, were treated with diasone. Of 44 cases who had diasone for 120 days or more, 11 per cent had minimal lesions, 55 per cent moderately advanced and 34 per cent advanced; 80 per cent had had the usual routine sanatorium treatment, whereas 18 per cent who took diasone were ambulant. Strict bed-rest was waived wherever possible and collapse therapy was withheld. Each patient was first given 0·33 gramme orally 3 times daily with meals. The average daily

intake for the test period was 0.9 gramme. Reactions to the drug (including one dermatitis) persisted for 2-4 weeks, after which they became slight or ceased. They were not irreversible or intolerable. Patients with fresh exudative lesions often showed an initial temperature rise and then a slow fall. Pulse rates all increased at first. About half of the group showed blueness of the face, lips and finger-tips. Nausea occurred in a quarter of patients but vomiting was infrequent. Headaches occurred in half the number of cases; 12 had photophobia, 6 diplopia and about one-third slight tremor. There was often an abrupt fall in the haemoglobin content of the blood and a fall of 1,000,000 in the erythrocyte count, which lasted for 5-7 weeks. There was not much change in the leucocyte count. There was no demonstrable correlation between the blood level of diasone and clinical progress. Slight to moderate resolution of infiltration occurred radiologically in 90 per cent of cases. There was accompanying increased fibrosis in 30 per cent, and 43 per cent of cavities disappeared. Within from 45 to 125 days 59 per cent of treated cases (including all minimal cases) became sputum-negative. Improvement was recorded as marked in 18 per cent, moderate in 50 per cent, slight in 25 per cent; 4.5 per cent were worse and 2.5 per cent showed no change. There were not any deaths. The greatest improvement occurred in the first 60-90 days of treatment. Non-pulmonary co-existent tuberculous lesions responded very favourably.

Promin tests.—Feldman, Hinshaw and Mann refer to previous reports which have shown that the expected course of experimental tuberculosis in guinea-pigs can be influenced favourably by certain chemical compounds, namely 4:4'-diaminodiphenylsulphone and certain derivatives of this substance, such as sodium *p*:*p*'-diaminodiphenylsulphone N:N'-didextrose sulphonate (promin) and disodium formaldehyde sulphonylate diaminodiphenylsulphone (diasone). These compounds are considered chemically as sulphones. The relatively high toxicity of both promin and diasone for human beings in doses therapeutically adequate has limited their clinical application. The authors report on a compound with the trade name of promizole (4:2'-diaminophenyl-5'-thiazolesulphone) which has a therapeutic efficacy for tuberculosis in guinea-pigs comparable to that of promin and diasone. The drug is reasonably well tolerated by guinea-pigs when given by mouth for prolonged periods. Some blood dyscrasia occurred but the changes were not critical and were reversible if administration was dropped. In experimental tuberculosis a daily dose of from 200 to 250 milligrams of promizole had a therapeutic efficacy comparable to a daily dose of from 400 to 500 milligrams of promin and was capable of influencing tuberculosis favourably although treatment was not begun until 6 weeks, 10 weeks or 14 weeks after the animals had been inoculated with tubercle bacilli. Prolonged administration of promizole induced diffuse parenchymatous hyperplasia of the thyroid, which was not irreversible.

Hinshaw, Feldman, and Pluetze report on the clinical use of promizole for 56 patients with pulmonary tuberculosis. About one-third of the number received sufficiently large doses to attain blood concentrations of the drug comparable to those found adequate in experimental tuberculosis of guinea-pigs. The dose suggested is 10-16 grammes a day orally. No serious toxic effects were found although some patients were so treated for 4 months. With these doses there is a blood concentration of the free drug which averages 2.6 milligrams per 100 cubic centimetres of blood. Promizole appears in the urine in rather large amounts, which indicates its relatively complete absorption. Usually more than 80 per cent appears as a hydroscopic conjugation product which does not produce concretions and renal damage. The urine of patients taking large doses often becomes pink. Slight transient cyanosis was seen occasionally. A mild erythema was seen twice, and two patients who were taking large doses vomited. There was not any leucopenia drug fever or any idiosyncrasy. Promizole is a fine white powder, incompletely soluble in water, with a bitter taste. It may be given orally in capsules or suspended in water or fruit juice, 4 or 5 times daily. Its use is still at an experimental stage.

Since 1938 it has been established that experimental tuberculosis in guinea-pigs can be combated successfully by certain compounds derived from 4:4'-diaminodiphenylsulphone, even if the treatment is delayed for as long as 6 weeks after experimental infection. The best known of these derivatives is promin. Feldman, Hinshaw and Moses have combined experiments with another derivative, namely disodium formaldehyde sulphonylate diaminodiphenylsulphone. Forty-two guinea-pigs were inoculated subcutaneously with a virulent strain of human tubercle bacilli. Of these 14 received treatment with the drug, beginning on the forty-sixth day after infection, 28 being used as controls. The drug was given orally with the food, each animal receiving 325-350 milligrams daily, which was about the limit of their tolerance. When the experiment was terminated 228 days after inoculation, 20 of the controls, or 71.4 per cent, had died of tuberculosis whereas only 2, or 14 per cent, of the treated animals had died and the cause of death in one of these was doubtful. The death rate amongst the treated animals was therefore one-fifth that of the untreated. Unfortunately all these diphenylsulphone derivatives are toxic to guinea-pigs and even more so to man and the measure of their toxicity appears to correspond with their effectiveness against tuberculosis. The toxic effect may be estimated by the lowering of the erythrocyte count and haemoglobin content, and by the increase in the reticulocytes. The drug under test is less toxic than the parent substance from which it is derived; it is also less effective against the tubercle bacillus.

Observation of pleural effusion cases.—Heaf and Hillingworth report on the work of the London County Council unit at Queen Mary Convalescent Hospital, Sidcup, for the observa-

tion, treatment and assessment of patients with pleurisy, pleural effusions and minimal pulmonary tuberculosis. Cases with sputum or post-primary parenchymatous lesions are not admitted, and no case which shows progressive pulmonary involvement is allowed to remain. The unit contains 130 beds. Attention is especially paid to previous illness and to the elimination of chronic sinus trouble in cases in which X-ray examinations show vague pulmonary shadows. Evidence pointing to a tuberculous origin of an effusion includes history of contact with the disease, a positive family history, previous erythema nodosum or phlyctenular conjunctivitis, sudden onset without pneumonia or rheumatism, especially if tuberculous hilar glands are found, and continuous raised pulse rate while resting in bed, as well as the demonstration of tuberculous infiltration in the lung parenchyma by X-ray examination. Patch and Mantoux tuberculin tests are employed, but gastric lavage has not been found to be of diagnostic assistance. Routine treatment of pleural effusions includes 6 weeks' rest in bed in all cases. After pulse and temperature have been normal for 2 weeks the patient is allowed up for short periods which are gradually extended, and light work or walking exercise is undertaken. X-ray examination and estimation of the blood sedimentation rate help to determine the rate of progress. After a patient has been up all day, he is advised to take a period of 'hardening off' at a seaside convalescent home or industrial settlement before he returns to work. In effusions the fluid is not aspirated unless it causes respiratory embarrassment, or unless its absorption is unduly slow. When a minimal lung lesion is found on the side of the effusion a phrenic crush may be given. If the lung lesion is progressive an artificial pneumothorax is established before the patient is transferred to a sanatorium.

Scope of pneumoperitoneum in pulmonary tuberculosis.—Rudman discusses pneumoperitoneum, its indications and technique and reports on 5 cases. The procedure was introduced by Joanides and Schlack as an adjuvant to phrenic neurectomy in 1936 and since then attempts have been made to extend its field of employment. Rudman is of opinion that its greatest usefulness still lies in its ability to enhance the value of the rise in the hemidiaphragm after phrenic interruption. Subsidiary indications for its use are (1) as an adjuvant to rest in bed in preparing a patient for radical chest surgery and (2) as a trial measure to determine diaphragmatic mobility prior to phrenic interruption. It has been found *per se* to be of very limited value. It is a far more formidable procedure than artificial pneumothorax and it must be done under conditions of rigid asepsis. The point chosen for the insertion of the needle is about one inch above and to the left of the umbilicus. Nitrogen was used by Rudman in preference to air and he advocates the use of a single Vim 19-gauge 2½-inch needle both for the infiltration of the abdominal wall with 2 per cent procaine hydrochloride (novocain) solution and for the introduction of the gas. A 3-way petcock is used, to which is attached a 5 cubic centimetre Lucr syringe containing the anaesthetic. As it is often impossible to tell when the peritoneum is punctured except by a sensation in the hands of the operator, trials may have to be made by allowing minute amounts of nitrogen to go through the tubing while the operator watches the water manometer; this will show a positive reading until the peritoneal cavity is reached and will then drop to zero or lower. As a rule 500 or 600 cubic centimetres of nitrogen are used for the initial installation. Four cases of air embolism, 4 cases of injection of gas into the spleen and one death from peritonitis have been reported, as have the occurrence of ascites and of peritoneal irritation.

Primary testing for tension prior to thoracoplasty.—It is essential, according to Vineberg and Kuntler, to distinguish tuberculous cavities, including residual cavities in which the pressure exceeds atmospheric pressure, from those which have lesser pressure, before thoracoplasty or drainage is selected as the first procedure. The tension cavities are maintained by valvular obstruction of their bronchi, reinforced by the traction of fibrosis. In all such cavities which exceed 2.5 centimetres in diameter the pressure should be tested by needling. Radiography is here inadequate. If the pressure exceeds atmospheric pressure drainage should be undertaken since the cavities are mechanically incapable of yielding to immediate thoracoplasty. The procedure is inappropriate to cavities with less than atmospheric pressure or to those near the hilum, as well as in the case of patients who are very ill, especially those with haemoptysis. Any free pleural space must be obliterated by injection of blood or some other fluid; if a pneumothorax has previously been produced the complete adherence of the re-expanded lung must be ascertained. Complications were absent when the technique advocated for the introduction of a drainage catheter was employed, a technique which eliminates the occurrence of haemorrhage. The use of a coagulating current applied to all exploring needles and the employment of suction syringes charged with saline solution prevent air embolism. The obliteration of pleural spaces obviates the occurrence of empyema. Twelve hours' daily suction, discontinued during the night, for 10 days was the general rule; the time for removal of the catheter was determined by radiographic disappearance of the cavity and by the absence of tubercle bacilli in catheter contents and sputum. The catheter is gradually withdrawn over a period of 3 weeks. Subsequent thoracoplasty in order to consolidate results is usually necessary. Large apical cavities in contact with the anterior pleura which show positive pressure require a preliminary anterior thoracoplasty. When the drainage is completed posterior thoracoplasty is undertaken. A 67 per cent success in cavity closure was attained in 24 cases treated according to these principles.

Suction drainage and thoracoplasty.—Brunner reviews the subject of suction drainage of cavities in tuberculosis of the lungs. Increase in size of a cavity is due not entirely to loss of

tissue but partly to pressure of the contents upon the adjacent lung with consequent atelectasis. The size of the cavity may thus be considerably reduced by aspiration. It is essential however that the intracavitary pressure should be reduced below that in the surrounding lung and this is possible only when the bronchus communicating with the cavity is blocked or is at least so greatly narrowed that it admits less air than the suction catheter removes. Before the cavity is punctured care must be taken to ensure that the overlying pleural space is obliterated, if necessary by preliminary injection of sclerosing fluids. Possible complications include pleural infection with resulting empyema. Monaldi, the inventor of the method, had 7 cases among his first 330 patients, of whom one died. Infection of the track through the chest wall is not uncommon. Severe bleeding and air embolism are rare. The length of time for which drainage must be carried on varies between one month and several years. It should not be discontinued until the amount of secretion has become minimal and tubercle bacilli are no longer present, and the use of the tube should not be left off abruptly; the original tube should be changed successively for shorter and smaller ones. Since closure of the efferent bronchus is essential for healing, various measures such as diathermy have been used to bring this about if it has not occurred naturally. Suction drainage gives good results in cases with isolated recent cavities and little or no tuberculous infiltration of the surrounding lung and is often successful in cases of residual cavity after pneumothorax treatment. For chronic cavitation suction drainage gives the best results when it is combined with thoracoplasty.

Total pneumonectomy: indications for its use.—Lorge and Dufault discuss total pneumonectomy in pulmonary tuberculosis and report on 3 cases. Rolley and Jones had already analysed data of 19 pneumonectomies for tuberculosis, including 4 of their own. The mortality was 40·2 per cent. Only 3 of the 11 survivors were considered to be well after the operation; 6 were improved. In the authors' opinion the operation should always be preceded by thoracoplasty with extrafascial apicolysis. On 2 of the patients in the cases here discussed partial thoracoplasties had already been performed, in addition to which one had had a phrenicectomy. Both these patients made a partial or complete recovery. On the third patient no plastic operation had been performed, but the authors do not consider that this affected the fatal issue of the case. The indication for pneumonectomy in tuberculosis is bronchial occlusion or stenosis not amenable to bronchoscopic dilatation, affecting the whole lung and eventually leading to pneumonitis, suppuration, bronchiectasis and abscess formation. In pulmonary tuberculosis the usual cause of occlusion is ulceration of a bronchus. Should only a branch bronchus be affected, lobectomy, the mortality from which is reported as ranging between 5 and 20 per cent, should be sufficient.

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LUNG DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 224; and Cumulative Supplement, Key Nos. 992–994.

Maligant tumours of lungs and bronchi

Primary

X-ray appearances.—Recent advances in the surgical treatment of primary cancer of the lung have given a new importance to early diagnosis which, once a matter of academic

interest, may now be of vital moment to the patient. Steenhuis quotes a series of 104 cases of which 21 were operable and 14 per cent were cured. Exact knowledge of normal and pathological anatomy is required to interpret radiographic appearances in the chest and the author has designed a transparent model of the thorax, made of glass and celluloid, for the purpose of assisting the radiologist to form an accurate mental picture of a growth of the lung and its relations to the principal bronchi and other structures. Most authorities now believe that cancer of the lung always originates in the mucosa of the large bronchi. It is certain that many growths are found in connexion with the larger bronchi and comparatively few in connexion with the smaller. In the early stages the growth does not appear as a shadow in the X-ray plate. It may however manifest its presence indirectly in diminution of the volume of the lung, in emphysema or atelectasis of a part of the lung, in dilatation of the bronchi behind the tumour, in bronchiectasis, in abscess formation and in thickening of the interlobar septa. In the later stages pleural effusion or metastatic deposits in the hilar glands may be observed but by this time the shadow of the growth itself will be visible. Reduction of the volume of a lung, when pronounced, results in displacement of other organs; in the earlier stages the results are diminished translucence and more distinct vascular markings. In the X-ray film atelectasis shows as an area of diminished translucency, emphysema as an area of increased translucency with diminished vascular markings. In order to demonstrate dilated bronchi and bronchiectatic cavities the use of contrast radiography is necessary. An abscess which arises in connexion with a growth gives X-ray appearances similar to those of any abscess and shows as a dense-walled cavity containing fluid and air. Planigraphy although still in its infancy seems likely to afford valuable information concerning the shape and size of the tumour and the presence or absence of atelectasis or of diminished lung volume. Bronchography may be of decisive importance for diagnosis, but as it is a more unpleasant procedure for the patient and is not free from danger it should be reserved for cases in which ordinary radiography and planigraphy have revealed some suspicious anomaly.

Surgical treatment of bronchial carcinoma.—Livingstone says that bronchial carcinoma is common in men, with fatal outcome. In his opinion surgical removal is the treatment of choice, as irradiation is palliative only. Early and accurate diagnosis is essential. Stained sputum, an abnormal cough, vague chest pains and increasing dyspnoea are 4 cardinal symptoms. Brock says that operation for removal of bronchial carcinoma is successful in only about 10 per cent of cases. A tiny growth in the lung may block a whole lobe and give misleading X-ray pictures, so that tumour dosage with deep X-ray therapy is difficult to assess in such cases. The accepted operation for bronchial carcinoma is the removal of the whole lung with the lymphatic glands, after dissection and ligation of the main vessels and bronchus. Lobectomy is an incomplete method as the lymphatic glands are not completely cleared. Lobectomy is however suitable in elderly people with peripheral tumours. Operation holds out hope for only 10 per cent of cases. After pneumonectomy some patients are able to do heavy work. The risk in the operation is that the pleural space may become infected and need draining for an indefinite period, but this is a small disability when compared to the great advantage of having had the tumour successfully removed. Ffrangcon Roberts discussed the value of radiotherapy for relief of symptoms, which may be considerable even in advanced cases; life may be prolonged by this treatment. Since he adopted a treatment technique of small fields his results have improved. Dobbie stated that in the course of 8 years 170 cases of primary carcinoma of the bronchus have been treated by X-rays in his units. Tomography should be used more in diagnosis; he found bronchoscopy to be somewhat disappointing. Seventy per cent of his cases were anaplastic tumours, which are unsuitable for operation. Dobbie gave palliative treatment—large fields and small doses—to 111 advanced cases; symptomatic relief was striking and some general relief was noted in 40 per cent of the cases. Radical treatment was used for small tumours and its effect was that a small volume of lung around the tumour was raised to a large dose. The patient wears a plaster jacket for treatment. A dose of 6,000 r in 5 weeks is given by means of a beam-directing device attached to the X-ray tube. Some of the patients were able to return to work and their life was prolonged. Harnett stated that out of 15,200 registered cases of cancer 1,023 were of bronchial carcinoma. The average duration of the disease was about 10 months.

Pulmonary asbestosis associated with carcinoma.—Homburger analyses the literature under the categories (1) fibrosis of the lung and (2) asbestosis of the lung, and refers to Lynch and Smith's paper in 1935 on bronchial carcinoma and epithelial hyperplasia. He finds that there are at least 19 cases known of asbestosis in association with primary pulmonary carcinoma, including the 3 cases reported here, and from his review concludes that neither from statistical calculations nor from purely morphological studies can it be decided that pulmonary asbestosis is an aetiological factor in pulmonary carcinoma. In 8 cases of pulmonary asbestosis 4 were combined with carcinoma. In the patient in the first case each lung weighed 700 grammes and the surface of the right lung was covered by white firm adhesions which bound it to the parietal pleura. The diaphragmatic surface showed a large number of firm white opaque nodules. In the patient in the second case microscopical sections of the lung showed that diffuse fibrosis of the lung was present. Metaplastic changes of the bronchial mucosa were seen in 4 out of 44 necropsies studied with special care from this point of view.

Necropsy statistics.—Steiner discusses the literature of pulmonary carcinoma and states that there is no doubt that the reported incidence of the disease has increased during recent years;

opinions differ whether this increase is real or only apparent. In a series of 5,515 consecutive necropsies at Chicago University between 1902 and 1941, Steiner found that the incidence of primary pulmonary carcinoma was 2.3 per cent and comprised 10.3 per cent of all tumours diagnosed as carcinoma. He divided the series into 5-year periods and found an apparent threefold increase between 1902 and 1941; at the same time there was an increase in all tumours found. Before 1927 the average incidence of all tumours found at necropsy was 20 per cent; subsequently it rose to 33 per cent. The probable explanation is that in 1927 the University of Chicago clinics were opened and attracted patients with a high tumour rate. Steiner next expresses the incidence of pulmonary carcinoma as a percentage of all tumours found over 5-year periods and notes only a slight increase in males and not any in females. He compares the incidence of other groups of tumours for which an increase is not generally claimed. There were even steeper rises in apparent incidence of colonic carcinoma and of intracranial tumours, but only a slight increase in the incidence of gastric and pancreatic carcinomas. The writer suggests that the apparent increase in the crude incidence rates of the above groups probably is due to the attraction to the University clinics of patients with such growths owing to especial interest being taken in these diseases. He concludes that his data show there to be only an apparent slight increase in pulmonary carcinoma.

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LUNG DISEASES: POST-OPERATIVE COMPLICATIONS

See also B.F.M.P., Vol. VIII, p. 235.

Massive collapse and atelectasis

Aetiology

Preventive treatment based on certain causes.—Chesterman describes two distinct types of collapse of the lung after lobectomy; these are based on the complete or incomplete airlessness of the involved lobe. The complete type, called apneumotosis, is caused by conditions which prevent circulation of air but not of blood. The incomplete type may be produced by fibrosis. Ligation of the pulmonary artery is followed by shrinkage and collapse of the lung. Post-lobectomy collapse is known to be caused by bronchial obstruction, pulmonary infection and fibrosis. Clinically, there appear to be 3 known factors in the production of post-lobectomy collapse: collapse due to pressure of a cyst, obstructive massive collapse and collapse due to progressive pneumonia of the chronic type ending in diffuse fibrosis. In order to prevent post-operative collapse it is most important to avoid infection of the lung by ensuring adequate drainage of the bronchi; this is best done by the use of the creosote chamber for adults. In children postural drainage is sufficient. Patients with a good cough reflex do not often suffer from post-operative infection. The pre-operative attempt to prevent collapse by treatment aimed at the formation of adhesions between visceral and parietal pleura has many disadvantages. Adhesions found at operation should be divided. Essentials in the anaesthesia for resection of a lung are prevention of anoxia, control of secretions and abolition of reflex disturbance. Spinal anaesthesia with intratracheal oxygen would appear to be a useful method. Post-operatively, the drainage tube should be attached to an apparatus so that forceful expiration and coughing take place against a known positive pressure. An oxygen tent should be used for the first few days. Regular coughing should be encouraged and later, breathing exercises.

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LUNG DISEASES: GENERAL

Primary pulmonary coccidioidomycosis

Epidemiology, clinical data and treatment

Importance in war-time.—Primary pulmonary coccidioidomycosis is not a common disease as its aetiological agent, *Coccidioides immitis*, can exist only under certain climatic conditions, but it assumes greater importance in war-time because of the presence of many troops in areas in which it is endemic and of the possibility of transmission of the disease by them to other regions at home or abroad. Goldstein and Louie report an epidemic of 75 cases representing the largest number hitherto treated by one group of investigators. Similar environmental conditions existed for all the patients, who were elements of a motorized division carrying out manoeuvres in an endemic area. Several thousand men were involved and the number of mild non-hospital cases is believed to have far outnumbered the 75 cases treated in hospital. The soil of the district consisted of fine sand and the movements of the vehicles created miniature sandstorms. The temperature ranged between 95° and 98° F. and the area was completely arid, all water being carried by the troops. The patients, who represented a loss to the service of about 5,500 man days, were admitted to hospital with symptoms of acute respiratory infection of different types. The diagnosis was confirmed by X-ray examination, positive cutaneous reaction to coccidioidin and serological and sputum tests. The intra-

cutaneous coccidioidin test was found to be of particular value, a negative result excluding the possibility of infection. Radiologically the usual findings were enlarged hilar shadows on one or both sides, with increased broncho-vascular markings in the involved regions. These appearances often clear very slowly; in such cases a patient may be returned to duty if all other signs have subsided. Pleural effusions occurred in 3 instances, cavitation in 3. Treatment is purely symptomatic. In this series the patient was kept in bed until all symptoms were absent and the blood sedimentation rate was 15 or less. The prognosis is good although the illness is long. Three and a half months after the commencement of the epidemic all the patients except one seemed likely to recover completely. The authors emphasize the great importance of careful selection of sites for military manoeuvres or camps.

Lung disease of boiler scalers

Clinical and radiological appearances

Dunner has collected material on an occupational disease of the lungs among boiler scalers, of which examples have been recorded by Cooke and Williams. Dunner reports on the lung lesions in 12 cases which occurred in males between the ages of 15 and 70 years and suggests that diagnosis will depend upon radiological examination. Clinically the symptoms may suggest tuberculosis, chronic bronchitis or emphysema; the symptoms and their duration do not bear any relation to the time spent on the work. Every boiler scaler is exposed to the dust of both the flue and the scale. None of the author's 12 patients was positive for tubercle bacilli. The radiological appearances vary; they may be unilateral or bilateral and show uniform mottling thus imitating miliary tuberculosis; cases with prominent fibrosis may simulate chronic miliary tuberculosis. The effect of the flue upon the lungs is known but not that of the scale dust; the desirability of chemical analysis in order to find out what kind of pulmonary lesion occurs in animals is pointed out. No statement about silica in the dust of boilers is made.

Treatment

Inhalational treatment

Use of a helium-oxygen apparatus.—In reporting 4 cases of serious respiratory disease Segal expresses his indebtedness to the researches and apparatus of Barach. Apparatus in general use permits concentrations of oxygen up to 75 per cent. The helium-oxygen apparatus now described delivers oxygen and helium and mixtures of the two in controlled proportions up to 95 per cent of oxygen with or without a positive pressure graduated up to 6 centimetres of water. There is a plastocole hood, sealed by a soft-rubber collar, which encloses the patient's head and a mask graduated for pressure up to 4 centimetres of water and adjusted so as to limit it to the expiratory phase only, if desired. Helium is biologically inert. A mixture of 80 per cent helium with 20 per cent oxygen is one-third lighter than air, and allows easier passage through constricted spaces. By adjusted mixture it should be possible to compensate for a 50 per cent reduction of the tubal respiratory tract. The degree of anoxaemia decides the oxygen percentage and the degree of obstruction decides the helium percentage. The mask is tolerated for certainly 3 days and the hood for still longer. The percentage of oxygen should diminish on transference of the patient from hood to mask or oxygen tent. In pulmonary oedema Barach compares the effect of inhalation under pressure to the control of capillary oozing by finger pressure. Nebulized adrenalin (adrenalin inhalant), aminophylline (theophylline in ethylenediamine) per rectum, dilaudid and iodides were supplementary agents employed to procure bronchial dilatation. Of the patients so treated the first was extremely ill with status asthmaticus, the second and third with bilateral virus pneumonia. These recovered. The fourth patient with a type VII pneumonia involving all lung tissue, after initial relief succumbed to septicaemia, renal insufficiency and endocarditis.

Partial lobectomy

Essentials for success.—The advantages of partial lobectomy in suitable cases are emphasized by Blades. Not only is the maximal amount of lung tissue conserved but with separate ligation of the structures at the roots of the lobes the incidence of post-operative putrid empyemas is greatly reduced. Both lower lobes consist of dorsal and basal divisions. The dorsal division can readily be localized at operation by occluding its bronchus and thus producing atelectasis of the part. The basal division is divided into 4 fairly constant segments, 2 anterior and 2 posterior. It is rarely wise to remove one segment alone because of the risk of leaving diseased tissue; but it may be possible to eradicate a diseased focus entirely by removing both anterior or both posterior segments. The middle lobe of the right lung is represented in the left lung by the lingula. Both are composed of 2 segments which can be separately excised although it is rarely wise to do so, especially on the right side. The apical divisions of the upper lobes are divided into 4 segments, and it is occasionally possible to avoid pneumonectomy by performing a partial lobectomy. Another purpose for which the operation may be employed is that associated with cases of suspected malignant tumour in which tissue for examination cannot be obtained through the bronchoscope and pneumonectomy is under consideration. Early operation is vitally important in bronchogenic carcinoma but the diagnosis should always be established microscopically before radical operation is undertaken. Successful use of partial lobectomy depends upon the fulfilment of the following requirements: (1) all diseased lobules must be recognized and removed; (2) the major bronchi and vessels of adjacent segments must be left intact; (3) satisfactory repair of the raw area of lung tissue must be carried out.

Careful preliminary localization of the disease by radiography including bronchography and by bronchoscopy is essential.

Thoracic surgery

Review of main lesions.—In the last 10 years surgery of the thorax has been widely practised, the most notable development being lung resection. Brock states that the thoracic surgeon must be an expert bronchoscopist, and must have a correct knowledge of the arrangement of the chief secondary bronchi. (1) In lung abscess a sound knowledge of the segmental anatomy of the lungs is essential for the prescription of correct postural drainage and for a correct and safe surgical approach for open drainage. Lateral radiographs are essential. Lung abscess rarely if ever occurs after an acute specific pneumonia; it is usually caused by a non-specific pneumonitis resulting from the inhalation of infected material from septic teeth or during anaesthesia. (2) In empyema after-treatment is of great importance. Much care and thought must be given to the correct placing of the drainage hole and to careful watching of the size, shape and extent of the healing pleural cavity. The tube, which may need frequent and patient readjustment, must be retained until the infected pleural space has been shown to be obliterated by complete fusion of the visceral and parietal pleurae. The recognition of the value of breathing and postural exercises before and after operation is a big advance. (3) In bronchiectasis the disability which ensues after lobectomy and pneumonectomy is usually small or non-existent. A successful lobectomy in a young patient should give rise to no disability whatever. (4) The surgical treatment of pulmonary tuberculosis is a vast and constantly enlarging subject. Air which is introduced into the pleural cavity benefits the patient only when it enables the diseased part of the lung to relax. Thoracoscopic division of adhesions which limit collapse of the lung is necessary. If a patient is likely to become fit for a thoracoplasty, extra-pleural pneumothorax should never be used in its place. Suitable patients should be submitted to thoracoplasty early. The chief difficulty in the way of permanent closure of a cavity by the Monaldi suction method is the persistence of a bronchial fistula. (5) The main problem to be solved in pneumonectomy for bronchial carcinoma is successful primary healing of the divided bronchus. Brock found that the operability rate in 187 consecutive cases of bronchial carcinoma was 8 per cent. He pays a tribute to the help given to thoracic surgeons by good radiology and anaesthesia.

Blades, B. (1943) *Ann. Surg.*, **118**, 353.

Brock, R. C. (1944) *Brit. med. Bull.*, **2**, 33.

Dunner, L. (1943) *Brit. J. Radiol.*, **16**, 287.

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Segal, M. S. (1943) *New Engl. J. Med.*, **229**, 235.

LUNG DISEASES: PULMONARY EMBOLISM

Radiological signs

Annular shadows in thorax

Caused by infarctions of bronchioles.—Thoracic annular shadows seen radiologically have been explained during the past 20 years as due to tuberculosis, pyogenic infection, necrosing growths, emphysematous pleural bullae, localized pneumothorax and bronchiectasis. Sante and Hufford report on 5 cases which displayed annular shadows coincident with systemic infection originating in tonsillitis, mastoiditis, rheumatic fever and other acute infective diseases. Soon after their onset, multiple rounded nodules about 6 centimetres in diameter appeared near the lung periphery but not on the pleural surface. On central rarefaction the cavity filled occasionally with fluid but usually with air. Such cavities, although doubtless communicating with the bronchi, did not vary with respiration and could not be filled by intratracheal injections of lipiodol. The rate of disappearance varied. In case (1) multiple shadows, accompanying tonsillitis and recurrent joint pains, persisted for at least one year. In case (2) mastoiditis, chronic otitis media and blood infection by haemolytic streptococci yielded to sulphonamide treatment; with recovery the 2 annular shadows disappeared. The staphylococcal septicaemia of case (3) which was successfully treated with antiserum (save that an eye had to be enucleated for panophthalmia) was accompanied by 2 annular shadows which had faded by the end of 6 weeks. The streptococcal pneumonic invasion with insidious onset in case (4) produced numerous annular areas in both lungs; these ultimately invaded the pleura and caused localized empyemas which necessitated drainage. Radiographic appearances in these cases do not resemble those of a pyogenic abscess. Their solid nodular origin differentiates them from emphysematous bullae. From the ordinary infarct they are distinguished by shape and position. Necropsy, after a fatal termination to pneumonia in case (5), lent support to the theory now put forward that these annular shadows reflect infarctions of the smaller terminal bronchioles resultant from embolism of the bronchial artery.

Sante, L. R., and Hufford, C. E. (1943) *Amer. J. Roentgenol.*, **50**, 719.

LUPUS ERYTHEMATOSUS

See also B.E.M.P., Vol. VIII, p. 244; Interim Supplement, No. 19*; and Cumulative Supplement, Key No. 1004.

Clinical types*Lupus erythematoses tumidus superficialis*

Response to tuberculin treatment.—A case of lupus erythematoses tumidus superficialis responding, although slowly, to tuberculin is reported on by Irgang. The patient, a woman of 28 years of age, had a bright red, oval tumour on the right cheek, measuring 2.5 by 1.9 centimetres, and raised 1.3 centimetres above the level of the skin. No other abnormalities were discovered on physical examination except excessive weight and a soft systolic cardiac murmur; radiography did not reveal any abnormality of the chest. The Kahn reaction was negative, the urine normal. Moderate secondary anaemia (65 per cent haemoglobin) and lymphocytosis of 47 per cent were present. An intracutaneous injection of 0.1 cubic centimetre of 1 in 1,000,000 old tuberculin solution elicited a strongly positive local reaction. Intracutaneous tuberculin treatment was given at weekly or bi-weekly intervals depending upon the degree of local reaction. At first the dose was 0.1 cubic centimetre of 1 in 1,000,000 solution; as the local response diminished this dose was increased. A strong reaction was aimed at on each occasion because it seemed to have a favourable effect. The treatment was continued for 14½ months, during which time the lesion had shrunk to about 10 per cent of its original size. The patient then grew tired of the treatment and ceased to attend.

Acute disseminated lupus erythematosus

General review of the condition.—Cluxton and Krause review the literature relating to acute lupus erythematosus disseminatus, which they define as a disease of unknown aetiology causing general damage to collagen and associated with widespread visceral lesions involving particularly the kidneys, lymph nodes, blood vessels and serous and endocardial structures. First described by Kaposi in 1872, the disease has been reported with increasing frequency. It is not common and occurs most often in northern climates and in white races. It shows a pronounced predilection for females, 77 per cent of patients being women. Usually it occurs in the second or third decade of life and very rarely under the age of 15 years. The course is variable, but in over 90 per cent of cases it ends fatally within 5 years as the result of some complication. It shows a striking tendency to appear or recur after exposure to sunlight or ultra-violet rays, X-rays or cold, or to the intracutaneous injection of tuberculin. It is associated with remittent fever. The skin lesions usually appear in the following order: face, neck, hands, extremities and trunk. They begin as well-defined erythematous patches which tend to coalesce and cover large areas and are characteristically located on the ends of the fingers and on the thenar and hypothenar eminences. The lesions may subsequently become papular, vesicular or bullous; as atrophy ensues a fine, grey, adherent scale appears. Mild itching or burning may occur during periods of increased activity. Visceral manifestations, which may precede the appearance of the eruption, include the following conditions. (1) Arthritis, with pain, swelling and tenderness of the larger joints; the pathological appearances are not specific. (2) Blood changes pointing to depression of haemopoiesis and including leucopenia, thrombopenia and moderate anaemia; the sedimentation rate is usually increased and remains high during clinical remissions; false positive tests for syphilis are not uncommonly obtained. (3) Inflammation of the pleura, pericardium and peritoneum, with effusion. (4) Changes in the endocardium; these are variable; they are said to occur in from 30 to 50 per cent of cases; myocardial changes are sometimes present, as is shown by alterations in the electrocardiogram; characteristic haematoxylin-staining granular bodies have been described as found in the endocardium; occasionally an atypical verrucous endocarditis is found. (5) Changes in the kidneys; in 70 per cent of cases a peculiar type of glomerular nephritis is seen, which gives a 'wire-loop' appearance to the glomerular capillaries. (6) Intra-ocular lesions; retinitis and papilloedema are particularly common. (7) Occasional cerebral involvement. (8) Lymphadenopathy; this is common. Treatment of lupus erythematosus disseminatus is purely symptomatic.

Allergy as the aetiological basis.—Fox cites as evidence that disseminated lupus erythematosus may have an allergic basis the case of a girl aged 17 years; after an injury she received a prophylactic dose of antitetanic serum and one week later a rash on the face developed with swelling of the ankles and of the interphalangeal joints of both hands. The joint symptoms gradually subsided during the following 4 weeks, but the rash persisted and after 2 weeks sore throat and diarrhoea developed, followed later by soreness and bleeding of the gums and by epistaxis. On admission to hospital one month after the onset of the illness the patient's temperature was 101° F. and a slightly raised, erythematous rash was present on the forehead, cheeks and bridge of the nose. No other abnormal signs were noted. The girl remained in hospital for about 3 months, with temperatures of 101° F. or over, then pneumonia and pericarditis developed; this was followed by peritoneal effusion and death. Necropsy disclosed vegetations on all four valves of the heart. Multiple necroses were present in the liver. In the kidneys many glomeruli were thickened, resembling the 'wire loops' described in disseminated lupus erythematosus. It is thought to be probable that the injection of a foreign protein initiated the disease.

Alteration in the albumin-globulin ratio.—Coburn and Moore have studied the plasma proteins in a series of cases of disseminated lupus erythematosus and have reached the conclusion that a relative increase in the gamma globulin content is a constant and significant finding. Fractionation of the serum globulins of 15 patients was carried out by Howe's method. All showed inversion of the normal albumin-globulin ratio, although the total protein was in most cases within normal limits. The average value for albumin (expressed in grammes per 100

cubic centimetres of serum) was 3.8 and for euglobulin 1. Repeated estimations made during the course of the disease showed that the inversion of the albumin-globulin ratio took place after the symptoms appeared and that the euglobulin rose as the disease progressed and fell as it resumed a quiescent state. In one case 4 years after recovery the albumin-globulin ratio was 1 : 1, the total globulin 3.8, the euglobulin 0.7. The greatest globulin values were observed in a fatal case which presented total globulin 4.8 and euglobulin 2.1 grammes per 100 cubic centimetres. Samples of plasma from 2 of the patients were examined by electrophoresis on several occasions. All the patterns showed an excessive amount of gamma globulin; the other globulin fractions were approximately normal. *In vitro* this gamma globulin fraction will give false positive Wassermann and Kline reactions; in the series now reported 11 patients gave positive reactions to the Wassermann test and 13 to the Kline test. False reactions are distinguished from true ones by their tendency to fluctuate widely in intensity week by week or even to disappear on occasion. The antibody responsible for these reactions has been found mainly in the gamma fraction, partly in the beta 2 fraction; this indicates that its mobility is between that of beta and of gamma globulin. The mode of production of this reactive protein is unknown.

Cluxton, H. E., Jun., and Krause, L. A. M. (1943) *Ann. intern. Med.*, **19**, 843.

Coburn, A. F., and Moore, D. H. (1943) *Johns Hopk. Hosp. Bull.*, **73**, 196.

Fox, R. A. (1943) *Arch. Path.*, **36**, 311.

Irgang, S. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 60.

LYMPHATIC GLANDS DISEASES

See also B.E.M.P., Vol. VIII, p. 264; Interim Supplement, No. 15*; and Cumulative Supplement, Key Nos. 1006-1009.

Subacute affections

Inflammatory diseases

Tuberculous adenitis.—Wilkinson and Cureton discuss the part taken by the lymphatic glands in preventing invasion of the blood stream by the tubercle bacillus and analyse the conditions found in 400 patients, mostly children, treated since 1930 at Black Notley Sanatorium, Essex, for tuberculosis of the cervical, thoracic or abdominal lymph glands. Further reports received in 1938 upon 101 of these patients showed that none had developed haematogenous or pulmonary lesions. In the authors' series of more than 1,000 cases of pulmonary tuberculosis only 5 patients had evidence of previous tuberculous adenitis. The lymphatic barrier reaches its maximum development about the twelfth year, and then shrinks at first rapidly, later more gradually. The catarrhal child who is the subject of lymphoid hyperplasia is rarely tuberculous, whereas in an adult bronchogenic tuberculosis may develop rapidly after primary infection. Immunity against tuberculosis can therefore be achieved better during childhood than in infancy or in adult life. The question remains whether active immunization in childhood will ever become possible.

Chronic affections

New growths

Diagnosis and prognosis in primary malignant lesions.—Valuable aid to prognosis and treatment has been afforded by the grading of carcinomas. Murray and Broders have investigated primary malignant lesions of lymphatic glands in order to obtain similar prognostic criteria. One hundred non-malignant glands free from inflammatory changes were obtained at necropsy and were examined microscopically. Two other series of 100 glands with inflammatory lesions and 379 glands with primary malignant involvement were similarly studied. It was observed that the ratio between the various cellular elements of non-inflammatory non-malignant glands varied greatly. The secondary nodules, or germ centres of Flemming, were absent in some glands in the first group; various types of giant cells were seen and mitotic figures were found outside the secondary germ centres. Invasion of the gland capsule by mature lymphocytes was not related to any malignant process. Lymph cords might be either present or absent in both malignant and non-malignant lymph glands. Increasing loss of cell structure and proliferation of a single-cell type was related to a malignant tendency and genuine pathological mitotic figures almost invariably indicated malignancy. In the grading of primary malignancy in lymphatic glands the various diagnostic criteria should be considered together. The histological grade in primary lymphosarcoma of lymphatic glands, exclusive of Hodgkin's type, has a positive relation to survival time. The survival rate for lymphosarcoma grade 1, exclusive of Hodgkin's type, appears to be similar to that for giant-follicle lymphoblastoma. The grade of malignancy in lymphosarcoma of Hodgkin's type has not any apparent relation to the survival time after histological diagnosis. According to the authors' observations the survival rate is approximately the same for all grades of primary neoplasm in lymphatic glands.

Carcinoma: metastatic spread in various conditions.—Whitcomb discusses the diagnosis of carcinoma of the cervical glands secondary to squamous cancer of the mouth and throat. Such metastasis appears with rare exceptions in the regional lymphatic gland of the tissue of origin of the growth and remains confined to it for a considerable period. Enlargement of the gland is usually gradual. The approximate percentage numbers of cases with glandular metastasis are 25 in cancer of the lip, 50 in cancer of the mouth and 75 in cancer of the throat. Clinical

diagnosis is often difficult or impossible—especially when, as may happen, the primary focus cannot be found—and should always be confirmed by microscopical examination. Specimens obtained by block dissection offer the best opportunities for studying involvement of the lymphatic vessels as well as the glands, although biopsy specimens may suffice for diagnostic purposes. Specimens obtained by needle aspirations are too small to yield consistently reliable results.

Murray, N. A., and Broders, A. C. (1943) *Amer. J. clin. Path.*, **13**, 450.

Whitcomb, C. A. (1943) *Amer. J. Roentgenol.*, **50**, 219.

Wilkinson, M. C., and Cureton, R. J. R. (1943) *Lancet*, **2**, 662.

MALARIA

See also B.E.M.P., Vol. VIII, p. 304; and Cumulative Supplement, Key Nos. 1018–1019.

Aetiology

Incidence

Suggested measures for prevention.—Bomford endeavours to assess the relative importance of (1) chance, (2) carelessness in the application of precautionary measures, (3) individual resistance and (4) loose living (alcohol, V.D. and bad discipline) on the incidence of malarial infections and relapses in military units. The observations were made on members of a military hospital unit in West Africa and, relative to factor (2), on information gathered from the records of 584 patients from other units who were carefully questioned about the observance of these measures. The conclusions reached show that (1) and (4) are not important but that (2) and (3) must be considered most fully in any attempt to control incidence and relapse. Discussing the measures to be taken to popularize the efficient application of anti-malarial precautions—for example nets, boots, suppressive drugs—among the troops, Bomford lays emphasis on the example set by higher ranks supplemented by explanation and education supplied by medical officers together with propaganda films and posters and, in a few cases, by disciplinary measures. With regard to the factor of individual resistance (3) he notes the detrimental effects of inter-current diseases such as diarrhoea particularly on the incidence of relapses and stresses the importance of maintaining the best standard of general health and particularly of adequate convalescence after attacks.

Parasitology

Experiments in breeding *Anopheles claviger*

The cages used by Davies for breeding *Anopheles (Anopheles) claviger*, Meigen, were wooden frames 5 feet long and 1 foot square, covered with sandfly netting. In experiment (1) 7 mosquitoes of each sex were introduced into the cage which lay with its long side on the laboratory bench. Some days later an arm was introduced on which the females fed avidly and at dusk a 25-watt lamp was placed at one end of the cage. Soon the males began a figure-of-eight dance. An hour later the females were seen also to be flying up and down the cage. Pairing ensued at intervals; the pairs immediately fell to the floor of the cage and parted within 30 seconds. This process was repeated on 3 successive evenings. In experiment (2) the cage was stood up on end and it was observed that the longer fall to the floor did not delay the separation of the pairs. In both cases about 70 eggs, black and fertile, were floating on a prepared bowl of water on the twelfth day. In experiment (3) shades of Cellophane, blue-painted Cellophane, typewriter carbon paper and waxed tracing paper were used in order to veil the lamp. Only the obscuration of the carbon paper inhibited copulation, therefore light was deemed to be essential. In experiment (4) the eggs were divided into 3 batches. Batch (a) in a water bath at the constant temperature of 19.5° C. hatched on the sixth day and passed through the 4 larval stages to the pupa stage in 24 days to become adult on the thirty-fourth day. Batch (b) in a fluctuating laboratory temperature averaging 11.9° C. hatched on the tenth day and became adult on the fifty-ninth day. Batch (c) in a fluctuating open-air temperature which averaged 10.5° C. hatched on the thirteenth day and became adult on the seventy-sixth day. The fluctuations in temperature in batches (b) and (c) probably account for widely varying time intervals between the different stages. The final experiment showed that rabbit's blood substituted for human blood as feeding material did not affect results.

Clinical picture

Associated conditions

General review.—Unless the very varied clinical manifestations of falciparum malarial infection are readily recognized, the early diagnosis and prompt institution of adequate treatment which may determine the outcome of a case cannot be made. The disease may be introduced into a country by persons coming from tropical areas, and Most and Meleney state that the possibility of malaria should be borne in mind when such patients are encountered, no matter what their symptoms may be. Specific treatment for malaria should be given in suspected cases until the diagnosis has been confirmed or disproved by the examination of thick and thin blood smears; the examination should be repeated every 12 or 24 hours if necessary. Initial symptoms of coryza may give place to cerebral symptoms such as stupor or coma; convulsions may occur and other signs of meningeal or encephalitic involvement may be seen. In cerebral cases parenteral injections of quinine dihydrochloride with dextrose and isotonic saline solution should be given; spinal drainage may be beneficial in comatose

patients. Nicotinic acid has been given to induce cerebral vasodilatation in order to facilitate the passage of quinine through the capillary vessels. Mental changes may take place and in such cases precautions must be taken against incipient mania or suicidal tendencies. In other cases the symptoms may simulate those of acute respiratory infection or of gastro-intestinal disorder. In the latter type there may be mild nausea, or severe vomiting and diarrhoea with localized or generalized abdominal pain; the possibility of bacillary and amoebic dysentery, intestinal obstruction and other acute abdominal conditions must be excluded and immediate and intensive parenteral administration of quinine is required; atebirin (mepacrine hydrochloride) should be given by intramuscular injection until the patient's condition improves and quinine dihydrochloride may be given intravenously; oral medication with atebirin (mepacrine) may then be continued. Totaquine is recommended in cases in which mepacrine is not tolerated. Quinine should never be given in the form of sugar-coated pills since absorption is thereby reduced. Falciparum malaria may occasionally simulate chronic or acute infection of the urinary tract, with the occurrence of blackwater fever. In severe cases jaundice, anaemia, azotaemia (uraemia) and anuria occur and death may result from anoxia or from complete urinary suppression. When severe anaemia is present blood transfusions may be given. In so-called algid cases the patient collapses and usually dies within a short time unless appropriate treatment is given immediately.

Diagnosis

Sternal puncture

As accessory to blood examination.—Aitken, and Rumball, Parsons-Smith and Nancekivell describe their experiences of the procedure of sternal puncture in malarial diagnosis. Examination of the blood was usually taken as decisive, 256 successes having been attained in 294 cases. Cases, clinically malaria, in which patients do not show parasites in the blood, often because they had been given quinine prophylactically, and atypical cases of patients admitted to hospital under diverse diagnoses, usually can be elucidated by sternal puncture. Aitken recommends a lumbar puncture needle with a guard half an inch from the point. Under local anaesthesia the needle is inserted by rotary movements into the centre of the sternum opposite the second costal interspace. Decreased resistance signalizes entry into bone marrow. The stylet is withdrawn and 1 cubic centimetre of fluid is aspirated. In 5 patients with *Plasmodium falciparum* in the blood, the sternal erythrocytes contained the parasite over twice as frequently as did the erythrocytes of the blood stream. The proportion exceeded 3 : 2 in 5 patients having *P. vivax* in the blood. In 95 cases, thick-drop examinations having been negative, 39 gave positive results on sternal puncture. The superiority of results from sternal puncture over results from blood concentrates was tested and proved. A few cases in which subcutaneous injection of 1 cubic centimetre of adrenaline had been tried with negative result, proved to be positive on sternal puncture. Sixty atypical cases gave 13 positive results to sternal puncture. Of the 47 negative patients 45 received other diagnoses. Pitfalls which await the inexperienced in reading the results shown by marrow films are distorted platelets, Howell-Jolly bodies and basophile erythrocytes irregularly stained. Case histories illustrate the vagueness of symptoms, including debility, headache, wasting, low pyrexia, indefinite history and lack of physical signs, which characterized one main type of latent malaria. In a second type the symptoms assumed a psychological disguise represented by neurasthenia or affective disorders. A third type comprised short fevers simulating sandfly fever and relapsing fever. In all such types, sternal puncture may often provide a positive diagnosis or a supplementary way of diagnosing cases in which peripheral blood parasites seem to be absent.

Treatment

Prophylaxis

Toxicity of atebirin (mepacrine hydrochloride).—Loughlin, Bennett, Santora and Mattucci publish the results of a comparative study of the toxicity of atebirin (mepacrine hydrochloride) of American and of German manufacture. Two groups of subjects were tested simultaneously, one consisting of 85 tuberculous hospital patients, the other of 64 healthy volunteers in a prison. Four different tablets were used: atebirin manufactured from American basic materials by American processes; atebirin manufactured from German materials by German processes; atebirin made from German materials by American processes; placebo tablets of similar appearance not containing any atebirin. Each tablet was marked by a different letter and neither investigators nor subjects knew what each contained. It was found that in the usual prophylactic doses against malaria (6 grains weekly) atebirin however prepared caused nausea, vomiting and diarrhoea in about 2 per cent of man days in both sick and healthy subjects, this figure representing the excess of incidence over that noted in the group taking placebo tablets. Tolerance was not significantly different with two different methods of dividing the weekly dosage, namely into 2 or into 4 separate doses. Not one of the healthy subjects was incapacitated from performing his assigned duties during the period of administration of the drug.

Prophylaxis and cure

Newer methods.—Talbot reports on antimalarial tactics at an outlying military base in a region of jungle and swamp which rendered successful mosquito destruction impossible. Further difficulties arose from a native population whose blood showed infection of 95 per cent. At first the military detachment here stationed received prophylactically 0.3 gramme of atebirin (mepacrine hydrochloride) twice weekly; when infection occurred malaria was severe

and obstinate. The naval detachment received treatment only on evident infection; although incidence was somewhat high the malaria was typical. Later, examination of all men of the naval and military forces concerned by the thick-smear method showed a percentage of infection in the naval detachment of 66 and in the army troops of 48. The medical officers became convinced that prophylactic medication was masking infection and that this was simultaneously damaging defence mechanisms. Therefore soldiers showing positive smears received one month's intensive quinine treatment. Sailors showing positive smears received similarly quinine and atebirin. Generally speaking, clinical malaria was prevented but occasionally quinine provoked chills and fever. Sporadic recurrences, especially of *Plasmodium vivax* infection, are inevitable. Atebrin given after quinine was occasionally ineffective and similarly quinine sometimes failed when atebirin succeeded. Atebrin never, quinine rarely, should be given intravenously and quinine should never be given subcutaneously. Intramuscular injections of either can be given until the patient can manage oral medication. The toxicity of plasmochin (pamaquin) is such as almost to prohibit its use. Malaria, like yaws, leprosy, trypanosomiasis and relapsing fever, causes positive Wassermann or Kahn reactions up to a frequency of 80 per cent. This phenomenon outlasts the cure of malaria by certainly 30 days.

Totaquine and atebirin.—Boyd considers that although a history of previous attacks, sojourn in malarial districts, inexplicable anaemia and splenomegaly or remittent pyrexia suggests malaria, the finding of the parasite in blood smears is the only complete justification of a diagnosis of malaria. Thick and thin smears on the same slide are desirable and failure to detect parasites in the thick smear within 5 minutes, or within 15 in the thin film, necessitates repeated examination on ensuing days. Ingestion of antimalarial drugs may make a latent condition bacteriologically undetectable for some days. The species should be identified and the density of parasites calculated, especially in the case of *Plasmodium falciparum*, the excess of which over 500,000 per cubic millimetre is a serious matter. The quartan parasite (*P. malariae*) rarely exceeds 10,000 or the *P. vivax* 50,000 per cubic millimetre. Daily smears provide the best record of successful treatment. Fever, anaemia and splenomegaly are the salient manifestations. The uniformity of paroxysmal pyrexia in vivax and quartan malaria, in which a temperature of 107° F. is not uncommon, contrasts with the irregular curve of falciparum infection in which 104° F. is of grave import. Splenic enlargement which persists after a first attack suggests continuing latent infection. Relapses and reinfections produce fibrous enlargement of indefinite duration. In the case of civilians, only totaquine and atebirin (mepacrine hydrochloride) remain available for oral administration. True prophylactic medication is non-existent, but a daily dose of 0.1 gramme of atebirin, by suppressing sporulation, prevents the development of acute attacks. In the treatment of the typical attack with totaquine, individuals over 12 years old receive approximately 0.6 gramme for each 50 pounds of body weight 3 times daily before meals for 7 days. Dosage for children is so graduated that infants receive one-tenth of this amount. Alternatively, atebirin 0.1 gramme is usually administered 3 times daily after meals and is continued for 4 days after subsidence of fever. Reduction for children tapers to a daily total of 0.05 gramme for those under one year. A doubling of the initial dosage is now recommended for adults. Intramuscular and intravenous injections of atebirin are restricted to cases of coma, hyperpyrexia and uncontrollable vomiting. If, concurrently with totaquine or atebirin, plasmochin (pamaquin) is employed as a gametocide the utmost circumspection is necessary.

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Bomford, R. R. (1944) *Lancet*, **1**, 750.

Boyd, M. F. (1944) *J. Amer. med. Ass.*, **124**, 1179.

Davies, R. A. (1944) *J. trop. Med. (Hyg.)*, **46**, 71.

Loughlin, F. H., Bennett, R. H., Santora, E., and Mattucci, S. (1943) *War Med.*, **4**, 272.

Most, H., and McIneny, H. E. (1944) *J. Amer. med. Ass.*, **124**, 71.

Rumball, C. A., Parsons-Smith, B. G., and Nancekivell, L. (1943) *Lancet*, **2**, 468.

Talbot, D. R. (1943) *J. Amer. med. Ass.*, **123**, 192.

MEASLES

See also B.E.M.P., Vol. VIII, p. 412; and Cumulative Supplement, Key No. 1027.

Clinical picture

Second attacks

Age influence.—During 1940 and 1941, during a study on the attack rate and incubation period of measles, Stillerman and Thalhimer observed 266 susceptible children exposed to the disease in family contacts in crowded tenement homes in New York City. The secondary attack rate in children aged from one month to 14 years is 75 per cent. Age is the chief factor influencing the secondary attack rate in these children. The rate was lowest for children in early infancy, highest for those between 1 and 7 years of age (80–90 per cent) and was 15 per cent for those from 10 to 14 years. Of 21 children aged from 6 months to 10 years who escaped measles on one exposure and were re-exposed, about half the number contracted the disease. Removal of patients to hospital after the appearance of the rash does not lower the secondary attack rate of intimately exposed susceptible children. In 9 families susceptible

children were in intimate contact with more than one patient with measles but this did not increase the incidence of the disease. The incubation period of measles was 10–14 days for 80 per cent of the contacts, 15–19 days for 14 per cent and less than 10 days for 6 per cent. The proportion of patients with an incubation period of 15 days or more was significantly greater in the 12-month to 23-month age group. The incidence of measles in the epidemic studied was the greatest ever reported in New York City. There was a greater incidence of measles among older children in suburban than there was among those in urban schools.

Treatment

Prophylaxis

Use of pooled convalescent serum.—Stillerman, Marks and Thalhimer report on a group of 502 closely exposed susceptible family measles contacts in New York City seen between 1938 and 1941, aged from 6 months to 15 years, who were given injections of pooled convalescent measles serum. There was a control group of 245 children of similar ages who were not given serum. In the control group of children aged from 6 to 11 months, one-third of the number did not have measles on first exposure; of children aged from 1 to 7 years 12 per cent, of those aged from 8 to 9 years 31 per cent and of the small group aged from 10 to 15 years 85 per cent, were immune. Up to 10 cubic centimetres of serum was given to children aged between 6 and 11 months, up to 15 cubic centimetres to those between 12 and 23 months and 20 cubic centimetres to those of 2 years of age and over. The optimum doses afforded complete protection to the three groups after an exposure of from 4 to 7 days. Of the 502 children, protection was complete in 50 per cent and useful modification of the disease occurred in 45 per cent. The rate of complete protection did not show any difference between the fourth and seventh day after exposure in the groups which received separately 5, 10, 12 and 20 cubic centimetres and in all dosage groups combined. On the eighth day after exposure the giving of serum modified but did not prevent measles. There was no difference in the rate of protection between contacts who had received injections when the patient with measles was removed to a hospital on the first or second day after the rash appeared and contacts when the patient remained at home throughout the illness. The passive immunity of contacts completely protected with 20 cubic centimetres of serum lasted for at least 2 weeks. In the average case catarrhal symptoms were most alleviated, fever least; the rash was the best indicator of the degree of modification. In treatment of measles contacts by convalescent serum injections, the age of the contact and the dose of serum were the two most important measurable factors. Complete protection is recommended for all exposed healthy susceptible children under 2 years of age and for contacts over this age who are ill. Modified measles is aimed at in healthy children aged over 2 years. For healthy contacts 4 years old and over, complete protection is not worth striving for. If modified measles is desired, a dose of 5 cubic centimetres is enough if given between the fourth and the eighth day after exposure for contacts up to 2 years of age, and 10 cubic centimetres for older children.

Dungal recounts experiences, prophylactic and curative, of convalescent serum in an Icelandic epidemic of measles. The serum, which was obtained from adult donors, was pooled. Their temperature after measles had been normal for a week and the first malaise dated back at least 14 days. The minimum dose employed was 2 cubic centimetres; 1 cubic centimetre was added for each year after the second until for adults 20 cubic centimetres was attained. The serum was administered subcutaneously to 203 individuals, of whom 30 per cent contracted measles and 70 per cent escaped. Its efficacy appeared to be profoundly influenced by the age of the patients. Of 115 children under 12 years old 96 escaped and 19 contracted measles, whereas of 45 individuals over the age of 12 years 25 escaped and 20 were infected. Of 45 individuals who contracted measles, 16 were affected within 10 days of injection. If the incubation period is regarded as 14 days, the disease was, in them, already established. A further 18 patients sickened between the 10th and 31st days after injection. The majority were doubtless infected before the injection, which delayed incubation. Fifty days or more passed before the remaining 11 sickened; the immunity had presumably lapsed, and it is deduced that, after 36 days of protection, these patients were exposed to infection approximately 14 days before the disease showed itself. The disease was mild and uncomplicated in injected persons. On an average their temperatures rose to 102° F. for 3–6 days, whereas patients who were not injected showed fever up to 104° F., which lasted on the average 8.5 days. Some evidence of curative effect was forthcoming when the serum was administered in the catarrhal stage and in one case, initially grave, the patient became convalescent 24 hours after injection of 40 cubic centimetres of serum. This aspect requires further investigation. If, in order to produce lifelong immunity, it is considered judicious to subject a child to a mild attack of measles, such an attack may usually be ensured by the administration of an adequate dose of serum 8 days after purposive exposure to infection.

Dungal, N. (1944) *J. Amer. med. Ass.*, **125**, 20.

Stillerman, M., Marks, H. H., and Thalhimer, W. (1944) *Amer. J. Dis. Child.*, **67**, 1.

— and Thalhimer, W. (1944) *Amer. J. Dis. Child.*, **67**, 15.

MEDIASTINUM DISEASES

See also B.E.M.P., Vol. VIII, p. 438; and Cumulative Supplement, Key No. 1028.

Classification**Tumours**

Three cases of ganglioneuroma.—Gray, Shepard and Dockerty discuss mediastinal ganglioneuroma and report on 3 cases observed at the Mayo Clinic in one year. Tumours in the anterior mediastinum are usually dermoids or thymomas. The middle mediastinum is the site for bronchial carcinoma and lymphosarcoma, whereas lymphosarcomas and tumours of neurogenic origin, such as the neurofibroma and the ganglioneuroma, are associated with the posterior mediastinum. Although the ganglioneuroma usually originates in the sympathetic chains some also arise from the central peripheral or parasympathetic nervous systems or from the medullary portion of the suprarenals. This tumour, which is rare in children and which is benign in older persons, has been found mainly in patients under 30 years of age. Often symptomless, many cases are first detected by thoracic X-ray examination. The tumour does not invade neighbouring tissues. Symptoms are indicative of pressure on adjacent vessels and organs. Dysphagia is rare. Protrusion into the spinal canal through an intra-vertebral foramen produces bizarre symptoms. Pyrexia of the Pel-Ebstein type has been observed in children with mediastinal ganglioneuroma. X-ray examination reveals a dense homogeneous ovoid mass arising from the posterior part of the thorax; it has a sharply defined convex lateral border and a flattened medial border. The adjacent vertebrae or ribs may show thinning or erosion. Apart from symptomless cases, the tumour may be diagnosed by signs of compression, the most common of which are brassy cough, dyspnoea and stridor, and by evidence which points to its benign character. When possible, complete excision by the posterior approach should be carried out. The principal surgical complication is haemorrhage from neighbouring large vessels. Subsequent recurrence with malignant change may supervene. The typical naked-eye and microscopical appearances are described by the authors.

Gray, H. K., Shepard, D. V., and Dockerty, M. B. (1944) *Arch. Surg., Chicago*, **48**, 208.

MEGACOLON AND ANAL ACHALASIA

See also B.E.M.P., Vol. VIII, p. 470.

Treatment**Operative**

Administration of spinal anaesthesia.—Hawksley reports on 12 cases of Hirschsprung's disease which were treated by administration of spinal anaesthesia. Only one patient did not benefit. The author classifies 6 patients as cured after from 9 months to 3 years of treatment and 3 as improving from 3 months to 7 months after; in 2 there has been insufficient time in which to judge the result. It appears that neither an immediate evacuation on the table nor a rapid improvement afterwards should be expected, and a long-term view is commended. Most of the patients showed no change for at least 2 months. Hawksley uses high spinal anaesthesia and administers percaine (nupercaine) to an amount either of 1 cubic centimetre per year age of the child or calculated on the Howard-Jones formula, whichever gives the smaller result. Ephedrine $\frac{1}{4}$ grain is first given intramuscularly. Then the warm light percaine (1-1500) is injected into the space between the second and third lumbar vertebrae in from 15 to 20 seconds, with the child sitting up. The child remains sitting for from 15 to 20 seconds, and is then placed on his back in the reversed Trendelenburg position. The position is maintained for 5 minutes, or until the child complains of 'pins and needles' in its hands. The table is then tilted in order to bring the shoulders downwards. Twenty minutes or more are required for the full effect to be seen; the characteristic picture is shown for an hour and a half. The legs and the abdominal and thoracic muscles are paralysed, and breathing is solely diaphragmatic. There is anaesthesia up to the nipple line and higher. A rectal examination is then carried out, and an attempt made to feel the pelvicorectal junction and to assess its degree of spasm. If it is contracted it should be dilated manually. After-treatment consists of wash-outs given on alternate days if no spontaneous bowel action occurs and liquid paraffin is administered nightly; the regimen is discontinued when the child returns home. In severe cases a weekly enema may be necessary. In unsuccessful cases spinal anaesthesia must be given trial 2 or 3 times before the treatment can be judged to have failed.

Hawksley, Margaret (1944) *Brit. J. Surg.*, **31**, 245.

MELIOIDOSIS

See also B.E.M.P., Vol. VIII, p. 485.

Clinical picture**Pyæmic form**

Bone and pulmonary lesions.—Mayer and Finlayson describe a case of chronic melioidosis with bone and pulmonary lesions which occurred in a military hospital in South Africa in a patient who had been in Singapore. Melioidosis, a disease which closely resembles glanders and was first recorded in Rangoon, is caused by the bacterium *Pfeifferella whitmori*. Most recorded cases are acute and rapidly fatal, but some chronic cases have been noted. The disease is said to be acquired by infection from rodents, possibly by infestation of food and

water supplies. In this case there was not any record of such infestation. The patient might have been infected by a tattoo artist in Singapore by whom he was tattooed. There was no history of venereal disease and Wassermann tests were negative. The illness started in June 1940 with pain in the lumbo-sacral region; it was insidious in onset, with irregular pyrexia and night sweats, and in the course of 2½ years multiple abscesses and sinuses of bone lesions—sacro-iliac, sacro-lumbar, dorso-vertebral and right hip-joint—developed as well as infiltration of the right lung base, hilar enlargement and apical pleural thickening. Although tubercle bacilli were not found and there was no cough or sputum the lesions were considered to be tuberculous, until at last an organism which resembled *P. whitmori* in almost every respect was isolated and an autogenous vaccine was prepared for treatment. With this and the surgical treatment required the temperature fell and the patient's condition improved. Cases of chronic melioidosis may occur in European troops when campaigning in regions in which the disease is endemic and may be mistaken for pulmonary or articular tuberculosis. Only two chronic cases have been reported in Europeans and the majority of reported cases have occurred in natives; it is possible that the former possess greater resistance to infection with *P. whitmori*, and that in them the condition may resemble the chronic granulomas.

Mayer, J. H., and Finlayson, M. H. (1944) *S. Afr. med. J.*, **18**, 109.

MENINGITIS

See also B.E.M.P., Vol. VIII, p. 495; and Cumulative Supplement, Key Nos. 1033–1040.

Pneumococcal meningitis

Course and treatment

Use of penicillin.—Cairns, Duthie, Lewin and Smith have treated 16 cases of pneumococcal meningitis with penicillin and had 12 recoveries. The sodium and calcium salts have been used intrathecally. Concentrated solutions of approximately 5,000 units per cubic centimetre were made in distilled water which, after Seitz filtration and assay, were diluted in water or normal saline to 250 or 500 units per cubic centimetre. The usual dosage was 3,000–4,000 units (4–10 cubic centimetres) per injection given daily, for a number of days which depended upon the bacteriology of the cerebrospinal fluid and the clinical progress. This dosage does not produce any recognizable impairment of nervous function. In the uncomplicated cases the course of treatment lasted for from 4 to 9 days. The total amount injected intrathecally varied between 10,000 and 85,000 units. In some cases penicillin was also given intramuscularly in doses of 15,000 units 3-hourly. In later severe cases a total dose per case of 50,000 units intrathecally and 500,000 units intravenously or intramuscularly was given. With the use of a sample of penicillin which contained 520 units per milligram, solutions containing 1,000 units per cubic centimetre were injected into the cerebrospinal pathways without any serious reaction. The penicillin solution was stored at 40° C. It was injected into the lateral ventricles through burr holes or into the lumbar subarachnoid space. Sometimes both these routes were used; the 2 fatalities probably occurred because the lumbar route only was used. The cisternal route was not used. One batch of penicillin when injected intrathecally produced sterile pleocytosis and brief symptoms of meningitis. An injection of 20,000 units in dilution of 1,000 units per cubic centimetre into the lateral ventricles in one case immediately produced a severe reaction. In one case in which the patient was convalescent from pneumococcal meningitis 100,000 units were injected intravenously without ill effect, and within the next 2 hours penicillin could be detected in the lumbar cerebrospinal fluid in sufficient amounts to inhibit the growth of staphylococci in a dilution of 1 in 2. Some cases have shown a tendency to relapse within 48 hours of the last injection. The authors propose in future to treat cases with sulphadiazine as well as with penicillin.

Cairns, H., Duthie, E. S., Lewin, W. S., and Smith, Honor V. (1944) *Lancet*, **1**, 655.

METABOLISM

See also B.E.M.P., Vol. VIII, p. 581.

Metabolism of food constituents

Protein metabolism

Hypoproteinaemia and hyperproteinaemia.—Wilensky states that plasma fibrinogen and plasma albumin appear to be formed exclusively in the liver, and plasma globulin chiefly in the liver and to some extent in the reticulo-endothelial system. The hepatic cells produce prothrombin in the presence of adequate supplies of vitamin K. The normal plasma protein level depends ultimately upon the continued ingestion of material which can be utilized for the formation of new plasma proteins, whereas the reserve body stores can supply a temporary replenishment but are readily exhausted. Proteins in adequate quality and quantity influence growth, maintenance and repair, reproduction and lactation, and antibody formation. They exert a protective action on the liver against injury of chemical and toxic origin, the amino-acids concerned being probably methionine and cystine. Protein has a lipotropic function, restricting intracellular deposition of fat. Clinical hypoproteinaemia may be found in under-nourishment, in digestive disease, in decreased intestinal absorption, in many varieties of liver disease, in renal conditions in which albuminuria is an important factor, in large haemorrhage and in the outpouring of serum into serous cavities. Hypoproteinaemia causes delay in

the healing of wounds. Post-operative hypoproteinaemia is common as a result of various causes, such as anaesthesia, the succeeding brief period of starvation, shock, fever and vomiting. The treatment will depend upon the cause of the deficiency. Adequate nutrition, rectification of alimentary tract disease, blood transfusion in cases of haemorrhage, removal and treatment of the hepatic toxic agents, thyroidectomy and treatment of nephritis are indicated for use in their individual spheres. In the event of lack of response or of urgency, parenteral replacement is called for and can be accomplished by transfusion of fresh whole blood or of plasma, or by the administration of amino-acids given intravenously or into the marrow bone subcutaneously; the use of the second route is not well tolerated in cases of severe damage to the liver. Reinfusion of ascitic fluid has also been employed. These findings are important in relation to the diet given before and after surgical interventions and to the nursing of the injured.

Carbohydrate metabolism

Decomposition of fibre in children.—Macy, Hummel and Shepherd investigated the value of complex carbohydrates in the diets of normal children. The fibre contents of the food and faeces of 18 healthy children between the ages of 4 and 12 years were analysed. The diets were comparable and contained common foods and were of constant quantity except for suitable adjustments to meet individual caloric needs. The children were observed for from 30 to 225 consecutive days. For the 18 children the mean values for total carbohydrate in the food ingested and in the faeces were 215.5 \pm 29.5 and 6.4 \pm 2.8 grammes respectively. The average daily intake of roughage from fruit, vegetables and cereals was 6.26 grammes. Of the total intake of fibre from 4 to 6 grammes was cellulose plus hemicellulose of which from 2.3 to 4.8 grammes disappeared during passage through the alimentary canal. The human body does not secrete an enzyme capable of dissolving complex carbohydrates, hence any resolution that takes place must result from the action of symbiotic micro-organisms. The completeness with which complex carbohydrates disappear from the alimentary tract is influenced by the variety and age of the preparation. There are wide variations in the ability of normal individuals to decompose the fibre of a diet. This was seen particularly among the younger children whereas there was less variation in the older group. Faecal cellulose plus hemicellulose per kilogram of body weight was related to faecal nitrogen, wet and dry weight. Positive and significant correlation coefficients were found for faecal cellulose plus hemicellulose versus faecal wet weight, faecal dry weight, faecal fat, faecal carbohydrate on dry weight basis and laxation rate. Negative and significant correlation coefficients were found for faecal cellulose plus hemicellulose versus ordinary ethereal sulphate and elimination time. These correlation coefficients were significant for the entire group of children, and partial correlation coefficients were significant when age and weight levels were held constant.

Interrelations of protein, fat and carbohydrate metabolism

Dangers of ketonaemia.—Administration of phlorhidzin and the consequent glycosuria result in removal of sugar from the blood, which in turn induces a compensatory increase in the breakdown of glycogen in the liver. Mirsky and Nelson state that when the liver reserves of glycogen are adequate the blood sugar remains relatively constant during and after a short period (6 hours) of phlorhidzin action. When the liver reserves of glycogen are inadequate, hypoglycaemia and ketonaemia develop as soon as a relatively small amount of sugar is lost from the body. A study of 52 normal and 26 diabetic children showed that removal by glycosuria of from 15 to 20 grammes of sugar from the normal child, or of a lesser amount from the diabetic child, resulted in liver glycogen depletion and in consequent development of hypoglycaemia or of ketonaemia. The loss of from 15 to 20 grammes of sugar by the normal adult does not produce such an effect but in the diabetic adult it results in a decrease in the blood sugar and in the development of ketonaemia. The younger the child the smaller is the relative reserve of glycogen in the liver, which accounts for the inverse correlation between the age of the child and the incidence of ketonaemia. In the words of the authors, fats do not 'burn in the flames of carbohydrates' but 'the flames of carbohydrate inhibit those of fat'. Any phenomenon which will increase the metabolic demand of the muscles for carbohydrate (such as high body temperature) or which will decrease the availability of carbohydrate for storage in the liver (such as vomiting) will favour the development of ketonaemia. Hypoglycaemia in such circumstances will cease when the rate of formation of sugar from non-carbohydrate sources catches up with the rate at which the liver loses its glycogen. This conforms with earlier observations that a fast for a short period (10–14 days) will produce hypoglycaemia in children within 3–8 days, after which the blood sugar returns to normal. It is emphasized that in the presence of any infection or metabolic disturbance in the child a constant adequate supply of exogenous carbohydrate must be provided. Frequent meals, given if need be by night as well as by day, should counteract the increased liability to ketosis of sick children.

Diet and sulphonamide action

Greisheimer, Haffkesbring and Wertenberger report on the influence of diet on sulphonamide action in over 400 rats. The experimental diets studied were high fat, high protein and high carbohydrate, and a control diet. The sodium salts of sulphathiazole, sulphadiazine, sulphapyridine, and sulphapyrazine were given intraperitoneally. On each diet the livers of rats given sodium sulphapyridine were lightest. With sulphathiazole an increase in blood sugar and a decrease in liver glycogen occurred, but the decrease of glycogen was small on the high

carbohydrate diet. With sulphadiazine there was only a very slight effect on blood sugar; as regards liver glycogen the high protein diet offered the least protection against the drug and the high carbohydrate the most protection. The giving of sulphapyridine had the most pronounced effect on blood sugar and liver glycogen. The increase in blood sugar was marked, particularly in rats on a high fat diet. When sulphapyrazine was given an increase in blood sugar resulted which was most marked in rats which were on the high carbohydrate diet. The decrease in liver glycogen was constant in rats on the control, high fat and high protein diets, but an increased glycogen was found on those on the high carbohydrate diet. Although the giving of sulphonamides influences carbohydrate metabolism, changes in blood sugar and liver glycogen are not parallel. Two different mechanisms seem to be involved. Sodium sulphadiazine with a high carbohydrate diet modifies carbohydrate metabolism least (in rats), therefore seems preferable to others.

Mineral metabolism

Acid and alkaline phosphatase.—Jaffe and Bodansky in a lecture read to the New York Academy of Medicine, state that phosphatase is known by its activity. The pH at which the optimum activity occurs gives a base for dividing it into alkaline phosphatase and acid phosphatase. The former is widely distributed in human tissues. It helps in the absorption of glucose and in the formation of osseous tissue. Acid phosphatase is found in the prostate after puberty as well as in the spleen and in the brain. It nearly always rises above the normal level in carcinoma of the prostate with metastases. Cachexia often shows low values even when there is malignancy provided there are no metastases, but a pronounced leucocytosis increases the value. High serum alkaline phosphatase value must be considered with the whole blood picture before diagnosis can be made. The same applies to hepatic disorders in which the raised alkaline phosphatase must be judged together with the cholesterol and other values of liver function. Serum alkaline phosphatase value may be high in early rickets. The authors found that osteogenic sarcoma may or may not show an increase of the alkaline phosphatase value. Primary tumours in the skeleton such as giant-celled tumours never raise the alkaline phosphatase value of the serum; nor does Ewing sarcoma, provided there are not many metastases in the liver. Metastatic skeletal tumours, unless they provoke bone formation, also do not raise it. Cases which do show metastatic bone formation have an increased alkaline phosphatase value. This increase even in severe cases is not often above 15 units unless the liver has many metastases. In systematized anomalies of skeletal development such as fibrous dysplasia of bone there is usually a rise in serum alkaline phosphatase. The general factor in increased alkaline phosphatase in the various skeletal disorders seems to be the new formation of osseous tissue, connected with disorder such as that which occurs in extensive Paget's disease. As would be expected, the healing of a skeletal disorder, for example rickets, is associated with a decline of the phosphatase value to normal, synchronizing with cessation of abnormal reactive osteogenesis.

Water

Causes and treatment of dehydration.—Morris, lecturing to the Royal Medico-Chirurgical Society of Glasgow, pointed out that the possession of a skin frees the mammalian organism from complete dependence upon a fluid environment but at the same time necessitates exact regulation of the body fluids. These are divisible into (1) intracellular water, amounting to about 50 per cent of the body weight, and (2) extracellular water, about 25 per cent of the body weight and subdivided into intravascular and extravascular categories. Each day secretions and excretions require from 4,000 to 16,000 cubic centimetres of water, all derived from a volume of fluid, the plasma, which rarely exceeds 3,000 cubic centimetres. The residue must be supplied by ingestion of water, oxidation of foods and tissue metabolism and a reserve is maintained in the interstitial spaces of the body to guard against wide fluctuations of the volume of intravascular and intracellular water. Clinical dehydration may be produced (1) by loss of relatively greater amounts of water than of sodium, as in profuse sweating; (2) by loss of greater amounts of electrolyte, either acid or base or both, than of water; (3) by shock, in which change of permeability of the capillaries leads to transference of water from plasma to tissue fluids. To combat dehydration the water and electrolyte content of the body must be restored, any disturbance of the acid-base equilibrium must be removed and the tone of the peripheral vessels must be restored or maintained. Intravenous infusion best meets the need. Fluid and electrolytes are supplied by 0.9 per cent saline; the addition of glucose is advantageous. Acid-base equilibrium is restored by sodium chloride provided that the kidneys are working properly, otherwise it is necessary to give an alkali associated with weak carbonic acid, for example sodium lactate. If there is pronounced failure of the peripheral circulation plasma should be given.

Greisheimer, Esther M., Hafkesbring, Roberta, and Werlenberger, Grace E. (1944) *Amer. J. digest. Dis.*, **11**, 13.

Jaffe, H. L., and Bodansky, A. (1943) *Bull. N.Y. Acad. Med.*, **19**, 831.

Macy, Icie G., Hummel, Frances C., and Shepherd, Marion L. (1943) *Amer. J. Dis. Child.*, **65**, 195.

Mirsky, I. A., and Nelson, W. E. (1944) *Amer. J. Dis. Child.*, **67**, 100.

Morris, N. (1943) *Lancet*, **2**, 91.

Wilensky, A. O. (1944) *Arch. Surg., Chicago*, **48**, 36.

METABOLISM, BASAL

See also B.E.M.P., Vol. VIII, p. 588.

Standard conditions for measuring basal metabolism*In children*

Standards for the basal metabolic rate of children of from 2 to 15 years of age inclusive have been determined by Lewis, Duval and Iliff from 1,007 estimations in 70 boys and 718 estimations in 57 girls. The methods of reference selected for fixing the standards were calories per hour per square metre referred to age and calories per hour referred to surface area, weight and height respectively. The first three methods exhibit a relatively low degree of dispersion about the mean; the latter gives more variable results but was included because it has been much used. The choice of method for the individual case depends upon the purpose for which the determination is required. Use of the method of reference which shows the lowest degree of dispersion gives the clearest picture of the deviation of the values in any individual child from those established for its group. A method which shows greater dispersion may however be useful for the study of an individual child's physiological relationships. When the degree of dispersion is taken as the criterion of selection the coefficient of variation may be used to compute the percentage deviation from the mean to be expected in normal individuals. The values for plus and minus three times the coefficient of variation will give a range including 99·7 per cent of normal individuals. The range is found to be ± 18 per cent when the first three methods of reference are used. For the fourth method the range is ± 22 per cent for boys and ± 21 per cent for girls. The body size of the child has an important influence on the basal metabolic rate, and the closer a child falls in height, weight and surface area to the average for its group the more nearly will his basal metabolism approximate to the mean.

Basal metabolism in disease*Rheumatism*

Effect of rheumatic toxin on thyroid gland.—Brown and Wasson have performed 154 basal metabolism determinations on 97 rheumatic children in an endeavour to throw light upon a possible effect of rheumatic 'toxin' upon the thyroid gland. The subjects were of both sexes and their ages ranged from 8 to 17 years inclusive. Early in the course of the investigation seasonal variations were observed which for purposes of analysis necessitated the setting of three arbitrary periods, namely July to December inclusive, January to March inclusive, April to June inclusive. The results showed that in a large proportion of the children the basal metabolic rate was below the normal range. Forty-five gave values on one or more occasions below -10 per cent and nine below -20 per cent. Values above normal were found in only 2 subjects. The average for the 97 children was $-7·6$ per cent and for all the 154 estimations $-8·7$ per cent, the lower figure resulting from the carrying out of repeated estimations in children with exceptionally low readings. In 33 of the children determinations were made in two or three of the seasonal periods. The average metabolic rate during the July to December period worked out at $-7·6$ per cent in 23 individuals; during January to March at $-8·3$ per cent in 20 individuals; during April to June at $-11·4$ per cent in 27 individuals. Of these 33 children 21 gave progressively lower values in these three periods; 7 showed an opposite trend and in 5 no regular sequence of values was noted. No significant difference in basal metabolic rates was noted at different ages. The authors suggest that the seasonal variations may depend upon the presence of continuous infection which becomes more active in winter and spring and subsides during summer and autumn.

Effect of drugs on basal metabolism*Iodine*

Studies in children with hypothyroidism.—Hamilton, Soley, Reilly and Eichorn have made use of radioactive iodine in the study of iodine metabolism in children with hypothyroidism. Ten children were observed for the investigation, their ages ranging from under 1 year to 19 years. Two had goitres, but no one had received treatment in the form of iodine or thyroid extract for at least 6 weeks before the tests were made. The children were given an initial dose of iodine in the form of sodium iodide in quantities of from 3·5 milligrams to 14 milligrams according to age. The uptake of the iodine by the thyroid gland in each case was measured by means of the Geiger-Müller counter. It was found that in the thyroid glands of children with hypothyroidism but without goitre the concentration of iodine was very small but in the 2 children with goitres the uptake of iodine was rapid and was relatively large, the curve representing the extent of concentration being similar to that seen in patients with hyperthyroidism. In these two children there was a loss of iodine from the gland during the 24 hours immediately after but the character of the iodine passing out from the gland was not investigated. Patients with goitre and with severe hypothyroidism are seldom seen except in areas of endemic goitre but it appears that in such patients if the iodine passing out of the gland after iodine administration is in the form of an active thyroid hormone, the thyroid gland should be able to function normally provided the intake of iodine is sufficient. After an interval of a few months 6 of the children including the 2 with goitre were given a second oral dose of radioiodine amounting to 0·1 microgram. With this dose the thyroid gland tissue concentrated a relatively larger amount of the iodine than with the former larger dose.

These extremely small amounts of radioiodine may be used to demonstrate the presence in the body of any thyroid tissue capable of concentrating iodine. Specimens of the thyroid glands were taken for biopsy from the two children with goitre and radioautographs were made. In both subjects most of the iodine was present in the cells rather than in colloid matter.

Brown, E. E., and Wasson, Valentina P. (1943) *J. Pediat.*, **23**, 19.

Hamilton, J. G., Soley, M. H., Reilly, W. A., and Eichorn, K. B. (1943) *Amer. J. Dis. Child.*, **66**, 495.

Lewis, R. C., Duval, Anna M., and Iliff, Alberta (1943) *J. Pediat.*, **23**, 1.

MIGRAINE

See also B.E.M.P., Vol. VIII, p. 604.

Aetiology

Vasomotor disturbance

Capillary behaviour and migraine.—Redisch and Pelzer studied the capillaries of the body surface with respect to their possible relation to the migraine attack. Capillary microscopy and photography depend upon the adoption of definite criteria for deciding the limits within which a capillary blood vessel may be called normal; however, slight changes in diameter, a wavy course of the capillary and irregularities in blood flow are so common as to suggest that they come within the bounds of normality. Impaired visibility of the surface capillary outlines, or 'blurring', was found during 142 migraine attacks in 118 patients. This change was simultaneous in the skin and in mucous membranes and the authors consider that technical difficulties as an explanation can be excluded. In 90 per cent of the patients there were changes in the configuration of the capillary loop; increased tortuosity of the limbs, increase in the number of crossings and the occurrence of knobbing in the limbs were all noted. Following upon an injection of ergotamine tartrate during an attack it was observed that the original blurring tended to alternate between clearing and indistinctness. To the fasting patient, 1,500 cubic centimetres of water were given orally and in 14 out of 15 subjects an abnormal excess excretion rate took place within the succeeding 4 hours; in 21 out of 29 experiments a migraine attack developed as this excess excretion subsided. During the period of urinary concentration which occurs when a small dry meal is taken after the consumption of the 1,500 cubic centimetres of water, half the number of patients showed marked blurring of the capillaries and complained of severe headache. In two instances in which ergotamine tartrate was injected intravenously at the height of an attack the relief of headache coincided with a dramatic resumption of diuresis. The authors consider that these experiments with forced water consumption indicate a definite relation between the fluid balance of the body, the state of the peripheral capillaries and the migraine attack. At the same time they observe that changes in the surface capillaries are not proof of similar changes in the cerebral capillaries.

Part played by steroids

Torda and Wolff have carried out experimental studies on migraine headache. In an attempt to isolate a pharmacodynamically active substance, specimens of urine from 18 non-migrainous subjects and from 12 patients with migraine were collected and the urine samples were injected into the rectus abdominis muscles of frogs. It was found that urine collected during attacks of migraine produced a greater degree of muscular contraction than did specimens collected during attack-free periods. Urine collected during the prodromal period of migraine induced the smallest contractions. The 17-ketosteroid content of the urine increased with the contraction-producing effect. The increase in the contractions caused by urine taken during an attack of migraine was not considered to be due to potassium, acetylcholine or histamine nor was it related to the specific gravity of the urine. It is suggested that steroid compounds may assist in the production of an attack of migraine by the activation of the effect of a locally produced vasodilator neurohumoral substance. The relation of the 17-ketosteroids to the attack of migraine is not yet clear. Possibly the increased excretion of such compounds has no direct relation to the headache mechanism; it may represent a secondary hypersecretion of the steroid hormones or a decreased retention of steroid compounds in the body tissues. It has been shown that migraine develops during or immediately after sustained tension, exhaustion, frustration or emotional conflict and that such stress alone may induce some increase in 17-ketosteroid output. It is not the severe pain *per se* which causes the increase. Cranial vasodilatation is responsible for the headache occurring in migraine and most of the steroid hormones cause dilatation of the capillary vessels of the skin.

Redisch, W., and Pelzer, R. H. (1943) *Amer. Heart J.*, **26**, 598.

Torda, Clara, and Wolff, H. G. (1943) *J. clin. Invest.*, **22**, 853.

MOTOR NEURONE DISEASE

See also B.E.M.P., Vol. VIII, p. 611.

Clinical picture

Upper motor neurone paralysis

Various methods of treatment.—McCarroll and Schwartzmann classify the causes of 1,720 cases of spastic paralysis and allied disorders, seen at a hospital for crippled children at St. Louis, as (1) extrapyramidal lesions, (2) cerebellar lesions, (3) impaired mentality and

(4) lesions of the pyramidal tract. Cases of extrapyramidal lesion, almost all of which were cases of true congenital athetosis, and cases of impaired mentality were eliminated to a total of 477 as they were considered to be unsuitable for operation, as also were 17 cases of Friedreich's ataxia and cerebellar diplegia. Nine cases of cerebellar disorder, mostly resulting from tumours, were referred to neurological surgeons. The entire group of pure extrapyramidal lesions is unsuited to orthopaedic surgery. Conservative treatment consists in special training and physical therapy designed to establish better muscle control and coordination. The desiderata held to justify operation are (1) adequate walking balance, (2) little or no athetosis, (3) mentality adequate for cooperation and (4) preferably satisfactory speech. Of 1,217 patients with pyramidal tract lesions only 437 fulfilled these requirements. The lesions can be classified as (1) traumatic, originating usually in injury at birth, (2) developmental, or (3) infective, following encephalitis. Of the results of 115 operations on the upper limb, most of which were for pronation of the forearm and flexion of the wrist, only 16 are classified as good, function having been improved and deformity corrected. Improvement of deformity without improvement of function was more common. Conversion of the pronator teres from pronator to supinator by transplantation gave most satisfaction in pronation deformity. In the lower limb surgical procedures are advocated for adduction and internal rotation of the thighs, for flexed knees, for contracture of the tendo Achillis and for certain fixed foot deformities. Whereas surgical results in the upper limb on the whole were unsatisfactory, operations on the lower limb showed success in 63.6 per cent of cases.

Treatment

Vitamin E

In amyotrophic lateral sclerosis.—Davison reports the results of the treatment in 10 cases of amyotrophic lateral sclerosis by a diet rich in vitamin E in the form of thiamin chloride, ephynal, *a*-tocopherol, whole wheat-germ oil and bile salts. Until quite recently it was universally agreed that this disease was not amenable to any form of treatment. Wechsler and others found that animals when deprived of vitamin E became paralysed and underwent atrophy and Davison and his colleagues found that except for one of the 10 cases there was not any clinical improvement among the patients treated with vitamin E. Histopathologically, however, in 6 of the intensively treated the destruction of the myelin sheaths and axis cylinders was much less severe than in the untreated patients; the dense gliosis usually present in amyotrophic lateral sclerosis was diminished or almost absent in patients receiving vitamin E. The lessened myelin sheath and axis cylinder destruction and the faint gliosis in these instances were perivascular and insular in distribution. Davison suggests the possibility that vitamin E treatment caused a reversal of the reaction of degeneration affecting simultaneously and nearly equally the damaged myelin sheaths, axis cylinders and glia in amyotrophic lateral sclerosis.

Davison, C. (1943) *Bull. N.Y. Acad. Med.*, **19**, 386.

McCarroll, H. R., and Schwartzmann, J. R. (1943) *J. Bone Jt Surg.*, **26**, 745.

MOUTH DISEASES

See also B.E.M.P., Vol. VIII, p. 620; and Cumulative Supplement, Key Nos. 1084–1090.

Lips

Tumours and cysts

Epithelioma and its treatment.—Whitcomb reports on a study of 56 five-year cases of carcinoma of the lip, involving the exposed margin and by metastases the regional lymph glands of the neck. After cancer of the skin it is the commonest type of malignancy occurring in men. It is a squamous carcinoma and as a rule grows slowly. Metastases to the regional lymph nodes appears in approximately 25 per cent of cases. The diagnosis should be easy. Keratosis may co-exist and be difficult to differentiate from the scaly type of cancer. A chancre may present temporary difficulty in diagnosis. An important feature is that those lymph nodes which are palpable may be free of carcinomatous infiltration whereas those which cannot be felt may contain cancer cells. Biopsy should always be performed before any type of treatment is given; the specimen may be obtained by aspiration with a needle and syringe, by a cut with a Silverman needle or an excision with a knife. Surgery, X-ray irradiation, radium therapy or electrosurgery may be used with equally good effects, if employed skilfully and correctly chosen for the individual case. Surgery is a more certain method than radium therapy. The carcinoma was excised in 41 of the 56 patients studied; 9 were treated with radium and one by radium therapy and surgery. In 5 cases a carcinoma of the lip had been destroyed before the patient was admitted. Since in so many patients metastatic nodes do not develop, Whitcomb considers prophylactic treatment by surgery or X-rays as unnecessary; insistence on return for observation of the neck is more desirable. The treatment adopted for the metastases which developed in 20 of the 56 patients was as follows: surgery alone, 12 cases; surgery and radium, 2 cases; surgery and X-ray irradiation, 4 cases; X-ray irradiation alone, one case. The survival rate of these cases after 5 years was 15 per cent, whereas that of the series without metastases was 83 per cent.

Stomatitis

Types of stomatitis

Epidemic stomatitis in African camp.—Jones, Armstrong, Green and Chadwick describe

epidemic stomatitis in an African camp which housed 10,300 men of varied North African and Eastern Mediterranean nationalities, of whom 17 per cent were affected. From December 1941 to March 1943 standard diet No. 1, which contained 1.61 milligrams of riboflavine, was issued and there was not any occurrence of stomatitis. Standard diet No. 2 was then substituted, deficiencies in which reduced the riboflavine content to approximately 1 milligram, and within 10 weeks stomatitis appeared. The unsuccessful administration of calcium lactate and of preparations containing vitamins A and D indicated that the deficiency was of the vitamin B complex. Nicotinic acid was ineffective but the daily administration of fresh yeast or of riboflavine was curative in 5 days. The issue of standard diet No. 3, which contained 1.73 milligrams of riboflavine, prevented further occurrences. The symptoms comprised soreness of tongue and lips, with slight trismus and excessive salivation; there was not any general malaise. The tongue showed first a reddened wedge which proceeded backwards from the tip. As atrophy increased redness diminished; this gave to the filiform papillae an appearance of a white mushroom and to the fungiform papillae that of a red mushroom. Atrophy progressed to the smooth shiny tongue of pellagra rather than to the magenta tongue which is reputed to characterize riboflavine deficiency, but other pellagrous changes were absent. The lips and cheeks displayed angular stomatitis and raw areas became coated with white soddened epithelium. The palate was rarely involved and the upper lip was notably immune. Examination by slit lamp was highly instructive. In patients submitted to detailed examination in a general hospital the blood count was uninformative, the gingivae normal and the mild vascular keratitis which was present in 75 cases did not exceed that of trachoma, with which these patients were universally affected.

Jones, H. E., Armstrong, T. G., Green, H. F., and Chadwick, V. (1944) *Lancet*, 1, 720.

Whitcomb, C. A. (1944) *Amer. J. Surg. N.S.*, 63, 304.

MUMPS

See also B.E.M.P., Vol. IX, p. 1; Interim Supplement, No. 12*; and Cumulative Supplement, Key No. 1092.

Complications

Genital organs

Treatment of orchitis.—McGuinness and Gall analyse an epidemic of mumps among white American troops which lasted for 30 weeks from November 1942 and affected 1,378 cases. Troops in the camp consisted of an infantry division from the Southern States and a group of other units of approximately equal strength mostly coming from the north and the west. The first group provided 84 per cent of the cases of mumps. Intercourse between the groups was unrestricted. In 2.4 per cent of the total number the salivary glands escaped; involvement of the glands was bilateral in 70 per cent of the remainder. Two-thirds of the number of cases were uncomplicated. In the remainder, 494 instances of epididymo-orchitis and 55 of meningo-encephalitis constituted the outstanding complications. These two conditions were sometimes co-existent. The orchitis was bilateral in 53 patients and in 13 the epididymis alone was affected. The patient who was ambulatory after the subsidence of fever was not found to be more liable to orchitis than was the one kept in bed for 2 weeks. The onset of orchitis in 82 per cent of instances was within 8 days of the onset of parotitis. Its occurrence after 14 days was unusual and late onset seemed to forecast a mild attack. Testicular support affords relief, as does incision of the tunica albuginea, which should however be reserved for severe unilateral orchitis and for involvement of the second testicle; it is performed in order to prevent bilateral atrophy with sterility. The complement fixation test assists diagnosis when orchitis or encephalitis occurs without parotitis. In the 55 cases which displayed encephalitis, headache was invariable and stiffness of the neck frequent. Lumbar puncture gave relief but sedatives were usually adequate and recovery was rapid. The severity of symptoms and the extent of pleocytosis in the cerebrospinal fluid did not prove to be commensurate. Definite pancreatitis was not encountered; there were 2 doubtful cases.

McGuinness, A. C., and Gall, E. A. (1944) *War Med.*, 5, 95.

MYASTHENIA GRAVIS

See also B.E.M.P., Vol. IX, p. 34; Interim Supplement, No. 11*; and Cumulative Supplement, Key No. 1100.

Morbid anatomy and pathology

Thymic neoplasm

Report of a case.—King describes a case of myasthenia gravis in a man of 27 years of age, who made a satisfactory recovery after the removal of a slightly enlarged but hyperplastic thymus gland. A positive Wassermann reaction was obtained in the blood but not in the cerebrospinal fluid. The giving of a course of novarsenobenzol (nevarsphenamine) did not improve the patient's condition. Observation made 2 months after the thymectomy showed that the patient no longer complained of fatigue or of bulbar or ocular symptoms, but there is no mention of examination at a later date than this. The association of thymic neoplasm or hyperplasia with myasthenia gravis is now well recognized. Success has been often reported

in the apparent cure of the disorder after operative removal of the thymus; deep X-ray therapy applied to the gland has not proved so successful. Experimentally it has been shown that injections of thymic extracts produce noticeable muscular weakness; furthermore, the muscle fatigue which is present after extirpation of the adrenal glands and which responds to the administration of adrenalin is also less after the removal of the thymus. King points out that a true neoplasm of the gland would not be expected to cause myasthenia gravis since tumour cells are proliferating but are not present in physiologically active secreting forms; many of the so-called adenomas are merely areas of localized hyperplasia.

Diagnosis and differential diagnosis

Prostigmin test and quinine test

Eaton reports that in the Neurological Section of the Mayo Clinic, two tests—with prostigmin and with quinine—are being used more and more often since experience with unusual manifestations of myasthenia gravis has created a great deal of suspicion concerning this disease. Myasthenia gravis is apparently the only disease which is characterized by muscular weakness which is made strikingly better by giving prostigmine (prostigmin methyl sulphate) and decidedly worse by administration of quinine. The disease may occur in either sex at any age between infancy and senility and it must be considered in the differential diagnosis in any case of objectively demonstrable weakness whether the weakness is generalized or is localized to only a few muscles. Myasthenia gravis is associated with exophthalmic goitre. Furthermore, myasthenia gravis must be considered in cases in which weakness is not demonstrable on muscle testing but in which the patient complains of tiring rapidly, although the majority of chronically fatigued patients are not the subjects of myasthenia gravis. The prostigmine test advocated by Viets and Schwab is the important single diagnostic help. It is helpful in 2 general circumstances, (1) to confirm clinical opinion and (2) as a means of ruling out myasthenia gravis. In the Mayo Clinic a modification of the technique of Viets and Schwab is employed. Usually hypodermic or intramuscular injection of prostigmine methylsulphate (prostigmin methyl sulphate) is given. Although the quinine test is not so widely known as is the prostigmine test, Eaton emphasizes its value as described by Harvey and Whitehill. The minimal and maximal amounts of quinine needed for the test have not been established; so far all patients with myasthenia gravis who have received as little as 2 doses of 10 grains each, with 3 hours between one dose and the other, have had definite effects an hour after the second dose had been given.

Treatment

Prostigmin

Effect of prostigmin combined with ephedrine.—The neuromuscular block in myasthenia gravis is sometimes ascribed to inadequate release of acetylcholine. Wilson and Stoner attribute it to a circulating curariform substance. The effects of prostigmin, attributed by them to the dual inhibition of cholinesterase and of this curariform substance, were investigated by the examination of blood serum (specimens withdrawn from the antecubital vein); it was administered alone and combined with ephedrine. Ephedrine alone did not influence cholinesterase and benefited one patient only. Subcutaneously administered prostigmin produced muscular improvement with relief of ptosis and dysphagia, but not of diplopia, lasting for 90 minutes. Cholinesterase activity reached a maximum inhibition of 49 per cent and stood at 24 per cent when symptoms reappeared. Combination of prostigmin with ephedrine enhanced improvement, prolonged it to 3 hours and abolished diplopia. Maximum cholinesterase inhibition was again 49 per cent; it decreased to 25 per cent at the return of symptoms. Parallel clinical effects, slower in development but more prolonged, resulted from oral administration. The maximum cholinesterase inhibition produced by prostigmin alone was 13 per cent only; it was slightly increased and noticeably prolonged by the addition of ephedrine but persisted at the same level on the return of symptoms. It is considered that the relation between clinical improvement and cholinesterase inhibition has not been proved, and that the reinforcement derived from ephedrine owes nothing to increased inhibition. Probably ephedrine prolongs the effect of adrenaline which is obscurely essential to the activity of prostigmin.

Thymectomy

Review of literature.—Hardymon and Bradshaw give a summary of the literature which deals with the value of surgical intervention in myasthenia gravis and describe 3 hitherto unreported cases which were treated in the North Carolina Baptist Hospital. In the literature approximately 50 per cent of cases showed improvement by surgery but of these new cases improvement was seen in one and not any improvement in two. The relation between myasthenia gravis and the thymus gland was first suggested in 1901. Cases occurred from time to time which showed thymus abnormality of some kind and sometimes improvement ensued on removal of the gland. From 1941 onwards definite attempts were made to influence the course of the disease by surgery, with varying success. The authors' first case was that of a woman aged 40 years with a history of weakness of 12 years' duration. At an exploratory anterior mediastinotomy no thymus material was found, and improvement in the patient's condition did not take place. The second case, a man aged 42 years, had a history of symptoms for 9 months. A well developed normal thymus gland was removed from the upper strait of the anterior mediastinum, and a circumscribed encapsulated benign tumour from the base of the aorta. The myasthenia gravis symptoms were much improved and the patient was able to

resume his former occupation, but was taking 30 milligrams of prostigmin bromide daily. An acute duodenal ulcer with severe haemorrhage developed later. In the third case, a woman aged 39 years with a history of a long remission, the removal of a mass of normal thymic tissue with a large fibrotic area which showed some areas of necrosis caused little appreciable change in the patient's condition. The pathological diagnosis was incomplete involution of the thymus.

Eaton, L. M. (1943) *Proc. Mayo Clin.*, **18**, 230.

Hardymon, P. B., and Bradshaw, H. H. (1944) *Surg. Gynec. Obstet.*, **78**, 402.

King, E. S. J. (1943) *Aust. N.Z. J. Surg.*, **13**, 129.

Wilson, A., and Stoner, H. B. (1944) *Lancet*, **1**, 429.

MYOPIA

See also B.E.M.P., Vol. IX, p. 66.

Ophthalmological features

In high congenital myopia

Gamble analyses 25 cases of high congenital myopia observed during the past 13 years. Fifteen of the patients had convergent strabismus, and all except 2 recovered. The strabismus, which was low in amount, cleared up in most cases when the refraction was corrected by the wearing of glasses. In discussing the cause of the strabismus, the author does not favour the explanation that the myopic child makes his binocular adjustment for close objects only, as in some of the children amblyopia developed, and in others, fusion was subnormal. A notable point was the very low annual rate of increase of the myopia, -0.18D per year. Conus was observed in 2 cases only. On account of this, as well as the very slow rate of increase of the myopia, the author advances the theory that the myopia is due to the fact that the lens is abnormally spherical and the antero-posterior diameter of the eyeball is not short enough to compensate for this. His conclusions are that (1) high congenital myopia and convergent strabismus are often associated; (2) the myopia is lenticular in origin and relatively non-progressive, at least up to the age of adolescence; (3) the convergent strabismus is of low degree, is usually corrected by glasses, and on the whole is relatively unimportant.

Gamble, R. C. (1944) *Amer. J. Ophthalm.*, **27**, 159.

MYXOEDEMA

See also B.E.M.P., Vol. IX, p. 69; Interim Supplement, No. 16*; and Cumulative Supplement, Key No. 1111.

Clinical picture

General signs and symptoms

Hyperactivity of thyroid gland without associated hypertrophy.—Many cases of localized or circumscribed myxoedema are not recognized clinically. Sunseri records a case of papulo-nodular myxoedema in a woman, aged 42 years, in whom lesions developed within 2 years after partial thyroidectomy had been performed for hyperthyroidism. When the papulo-nodular lesions appeared the patient had an increased basal metabolic rate, tachycardia, exophthalmos and oedema of the legs. These signs suggested recurrent hyperthyroidism but were attributable to hyperactivity of the pituitary gland. The condition was not strictly circumscribed myxoedema because the cutaneous involvement was extensive; the terms, mucoid papular disease and lichen myxoedematosus, have been suggested as being applicable. The condition is the result of endocrine disturbances similar to those causing the ordinary type of circumscribed myxoedema, with plague-like lesions confined to the lower extremities. In the author's patient the initial oedema involving the legs and preceding the eruption may have been part of the myxoedematous syndrome. It is suggested that there may have been over-activity of the pituitary gland without associated hypertrophy (as shown by X-ray examination). The normal size of the gland may explain the absence of glycosuria, so commonly found in association with hyperactivity and overgrowth.

Myxoedema and anginal pain in the elderly patient.—It has long been known that ageing myxoedematous patients may also have symptoms of arteriosclerosis, hypertension or coronary artery disease. Peel reviews the types of anginal pain that may occur in myxoedema and discusses the effect of thyroid gland administration. He points out that it has been generally agreed that thyroid medication in myxoedematous subjects tends to aggravate co-existing anginal pain but that since 1924 reports have been made discrediting such an assumption. From a study of 60 cases of myxoedema the author concludes that several types of associated anginal pain may occur. Angina of effort commonly develops as a result of co-existing independent cardiac disease and less often in uncomplicated myxoedema. In the former event the pain may be aggravated, alleviated or unaffected by thyroid administration. In many cases there is an optimum dose which gives relief to the patient but any increased amount induces more severe pain. A persistent cardiac ache or pain which is made worse by exertion and which may be associated with collapse attacks, occurs in some patients with subclinical myxoedema and is termed the 'abortive myxoedema heart of Zondek'. The condition is relieved by giving thyroid gland extract but if it is unrecognized and untreated typical clinical myxoedema or angina of effort may develop. Spasmodic angina occurred in 2 cases in the

author's series; both patients may have had incipient hypertension but neither had any obvious complicating cardiac lesion. In one of these cases there may have been associated hypoglycaemia. In the other case anaemia was a complicating factor and when this was treated the patient's anginal attacks ceased. The author concludes that anginal pain in a myxoedematous patient does not contra-indicate cautious thyroid administration. The possibility of psychogenic pain must be considered in some cases of myxoedema.

Metabolic changes

Urea clearance.—Beaumont and Robertson publish a further study of renal function in myxoedema. Previously they described a case of pituitary hypothyroidism in which renal impairment was a prominent finding. The authors have now investigated 7 cases of myxoedema and observations were made before and after adequate thyroid gland administration. The later observations were made 3 months after treatment was started when the basal metabolism had become constant on a maintenance dose of thyroid extract. It was found that the urea clearance in myxoedema is low, rises after adequate thyroid treatment but still remains subnormal. Water excretion is normal and thyroid treatment does not cause any significant change. Myxoedematous subjects are able to concentrate their urine as efficiently as do normal persons. After thyroid administration the urinary specific gravity is lowered but not apparently as a result of diuresis. Chemical and microscopical urine examination did not demonstrate any other evidence of renal impairment in the authors' cases.

Treatment

Optimum dose of thyroid extract

Winkler, Criscuolo and Laviets, struck by the difference between the extreme sensitivity to thyroid extract of myxoedematous patients and the tolerance shown by many non-myxoedematous people, have studied the response to the administration of thyroid extract of 28 patients with pronounced myxoedema. The basal metabolic rate was determined at intervals over a period of months or years and correlated to the dose of dried thyroid which the patient had been taking during the previous month. Two readings were taken and if the difference exceeded 5 per cent a third reading was obtained. In each case the daily dose of thyroid extract was kept constant for a month before the determinations were made. It was found that the dose necessary to restore the basal metabolic rate to normal varied from 1 to 3 grains of U.S.P. dried thyroid extract daily; the majority of patients required about 1½ grains. The thyroid requirements tended to be somewhat higher in heavy people, but this correlation was very irregular. In some patients they varied from time to time. No evidence was obtained that tolerance to dried thyroid extract is ever developed. The relation between the basal metabolic rate and the daily dose tended to be linear at least so long as the rate was below normal.

Beaumont, G. E., and Robertson, J. D. (1943) *Brit. med. J.*, **2**, 578.

Peel, A. A. F. (1943) *Brit. Heart J.*, **5**, 89.

Sunseri, J. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 70.

Winkler, A. W., Criscuolo, J., and Laviets, P. H. (1943) *J. clin. Invest.*, **22**, 531.

NARCOLEPSY AND CATAPLEXY

See also B.E.M.P., Vol. IX, p. 91.

Nature of narcolepsy

Relation between narcolepsy and epilepsy

Electroencephalograms in ten cases.—Cohn and Cruvant conducted a clinico-electroencephalographic study in order to establish a relation between narcolepsy and epilepsy. In early sleep, whether physiological or narcoleptic, the characteristic encephalographic pattern is of the low amplitude, high frequency type; as sleep progresses slow wave discharges dominate the record and in deep sleep discharges at the rate of 14 per second occur as a transient phenomenon. Ten cases are recorded in 5 of which the attacks of irresistible sleep were associated with periodic cataplectic muscular phenomena induced by affective stimuli. The basic electroencephalograms, taken between the intervals of 'sleep', showed no wave pattern characteristic of the narcoleptic syndrome. The proportion of alpha frequencies varied from complete dominance to almost complete absence. The abnormal wave forms observed in the majority of the records were similar in all essentials to those obtained from epileptic persons. Isolated bursts of high voltage slow waves occurred in 4 cases within from 2 to 4 minutes after the start of the recording and were in no way associated with clinical or encephalographic evidence of sleep. Two cases demonstrated the 'epileptic' response to hyperventilation. The similarity of the records in narcoleptic seizures in the authors' cases to those of normal sleep indicate that the former are manifestations of physiological sleep, albeit inappropriate. Cohn and Cruvant in view of these findings suggest that hypnolpsy is a more appropriate designation for the sleep component of the narcoleptic syndrome. The conclusion arrived at is, that since the electroencephalographic abnormalities observed during the interscizure phase of narcolepsy appear qualitatively similar to those associated with epilepsy, Wilson's theory that the narcoleptic syndrome is a member of the family of epilepsies is confirmed.

Cohn, R., and Cruvant, B. A. (1944) *Arch. Neurol. Psychiat., Chicago*, **51**, 163.

NECK: TUMOURS AND OTHER MORBID CONDITIONS

See also B.E.M.P., Vol. IX, p. 104.

Wounds of the neck (out throat)**Treatment**

Laryngeal moulds.—Jackson and Jackson present the results of clinical observations on industrial, criminal, accidental and suicidal trauma of the larynx. The authors classify the causes of laryngeal trauma and discuss the pathological considerations of occlusion of the lumen of the larynx. The symptoms may not be suggestive of laryngeal injury but examination of the larynx is essential in every case of injury to the head or neck. In the early stages of laryngeal injuries the prognosis as regards life depends mainly upon the availability of surgical care; with prompt adequate surgical treatment few patients die from laryngeal complication. Tracheotomy may be required for emergency control of haemorrhage even when dyspnoea is absent. Early low tracheotomy is indicated in most cases of endolaryngeal injury. In lacerated wounds of the neck a cannula should not be worn in the wound for longer than a few hours, if it is worn at all. Debridement within the larynx is contra-indicated. The cervical wound should not be closed completely; any large passage into the larynx should be packed open until perichondritis and chondral necrosis are controlled. The laryngeal cartilage should not be stitched. When the food passages are opened a nasal feeding catheter should be used until repair is effected. Light sparing dustings of sulphonamide compounds may be used on mucosal wounds and care must be taken to prevent entrance of excessive amounts of the powder into the air or food passages. In laryngeal fractures and crushes a core mould should be used as an internal splint in order to maintain a sufficiently large lumen and to restore form. Normally such moulds can be introduced within from 7 to 14 days after the occurrence of the injury in order to prevent chronic laryngeal stenosis. Pneumonia and oedema of the lungs are very rare complications. Psychical trauma with vocal manifestations associated with laryngeal injury is in nearly all cases curable by psychical treatment.

Jackson, C., and Jackson, C. L. (1943) *Arch. Otolaryng., Chicago*, **38**, 413.

NEPHRITIS AND NEPHROSIS

See also B.E.M.P., Vol. IX, p. 134; and Cumulative Supplement, Key Nos. 1131–1141.

Morbid anatomy**Pathological classification**

Differentiation of main types.—The end results of varieties of advanced renal disease are clinically so similar that the clinician cannot accurately foretell what the pathological findings will be. Mansfield, Mallory and Ellis report on a study of renal infection which emphasizes pyelonephritis as a forerunner of hypertension. The suggested nomenclature is (1) glomerulonephritis, acute and chronic, (2) nephrosclerosis, benign and malignant, and (3) pyelonephritis, healed and chronic. Glomerulo-nephritis connotes active or healed inflammatory processes which affect the glomeruli, but it is probable that formerly many cases of pyelonephritis and malignant nephrosclerosis were included in this classification. The gradations from the large smooth yellowish kidney of subacute glomerulo-nephritis, with glomeruli showing cellular proliferation, fatty tubules and oedematous interstitial tissue, are not sharply demarcated from the pale contracted granular kidney of chronic glomerulo-nephritis, with fibrosis of glomeruli and interstitial tissue and with atrophied tubules. In the authors' series of 59 cases an infection was traced to have been present before glomerulo-nephritis developed in 90 per cent of subacute and in 30 per cent of chronic cases. Albuminuria, microscopical haematuria, pyuria and casts were maximal in the subacute and of high degree and common occurrence in the chronic condition. The malignant form of nephrosclerosis showed hyperplastic, probably fibroblastic, endarteritis, whereas the benign form showed a hyaline type. The urinary abnormalities in both forms ran parallel and ranged from a urine almost normal to a urine resembling that of glomerulo-nephritis, but the earlier onset, a survival rarely exceeding 2 years and the invariable papilloedema of the malignant type contrasted with the phenomena of the benign type. Both the healed and the chronic forms of pyelonephritis showed scarred or contracted granular kidneys. Evidence of infection provided by the finding of leucocytes, and even organisms, in the interstitial tissue differentiated the chronic from the healed form. There was rarely a history of acute pyelitis. With the exception of chronic pyelonephritis, high arterial tension pervaded all types and rose to its maximum in malignant nephrosclerosis. On the average, death terminated glomerulo-nephritis before the age of 35 years, malignant nephrosclerosis and healed pyelonephritis before the age of 42. Benign nephrosclerosis occurred after the age of 50 and chronic nephropylitis irrespective of age.

Treatment**Glomerulo-nephritis**

Acute and chronic stages.—In an article on the modern treatment of nephritis Micks defines acute nephritis as an illness with an abrupt onset and with characteristic renal and cardiovascular symptoms. No known treatment succeeds in raising the recovery rate in acute nephritis, so spontaneous recovery must be awaited. Rest in bed is usually necessary but should be continued only until diuresis occurs and the blood pressure returns to normal. In order to lessen oedema the intake of fluids and of sodium salts should be restricted. There is

not any evidence that a low diet is necessary. Saline diuretics, sodium compounds or potassium compounds may all be given. Mercurial diuretics are certainly useless and probably harmful; purine diuretics are useless although not dangerous; sulphonamides may be dangerous. In the treatment of acute cases which pass into the chronic stage it is generally agreed that restriction of the patient's food intake is not advisable. In chronic nephritis there is not any recovery from true nephritic uraemia but if there is a possibility that the condition is due to dehydration uraemia, salines should be administered. Micks considers that morphia should be given whenever there is associated cardiac distress, although on account of its depressing effect on respiration and its tendency to cause vomiting it should be given with care. The chronic nephritic patient with gross generalized oedema is often greatly benefited by a high protein and a sodium poor diet when a low serum albumin is one of the factors in the causation of the oedema. The value of lumbar puncture in either true or false uraemia, of magnesium sulphate given intravenously in true uraemia, of mercurial diuretics in the hypertensive heart failure of chronic interstitial nephritis and of sulphonamides in urinary infections, are discussed.

Mansfield, J. S., Mallory, G. K., and Ellis, L. E. (1943) *New Engl. J. Med.*, **229**, 387.

Micks, R. H. (1943) *Practitioner*, **151**, 321.

NERVE INJURY AND REPAIR

See also B.E.M.P., Vol. IX, p. 160; and Cumulative Supplement, Key Nos. 1142–1144.

Symptoms of nerve injury

Motor disturbances

Effect on certain muscles.—Meadoff and Gray emphasize the importance in medical practice of injuries to the brachial plexus, and describe a varied group of cases as seen in an industrial practice over a period of one year. The majority of lesions were produced by traction injuries of the brachial plexus and involved the entire plexus or individual nerves such as the long thoracic, the axillary and suprascapular. Treatment was conservative; physiotherapy, especially faradic stimulation, was employed. The brachial plexus is held firmly at two points, at the transverse processes and below the clavicle, by the prevertebral and clavicular fascias respectively. The middle part is surrounded by blood vessels and is the site of haemorrhage but seldom of the traction type of injuries. The present theory is that the majority of injuries occur either as root lesions or as terminal nerve lesions in the infraclavicular region. In abduction the pectoralis minor muscle acts as the fulcrum for the plexus, and in adduction, the scalenus anterior. An interesting example of post-serum neuritis and an unusual case of bilateral deltoid paralysis due to chronic arsenical poisoning are also presented. The theory that the scalenus anterior syndrome is attributable to the compression of the lower trunk of the brachial plexus and the subclavian artery between the posterior and lateral borders of the scalenus anterior muscle and the body of the muscle, is criticized; the authors consider that a traction mechanism is involved. The contraction or contracture of the scalenus anterior results in elevation of the first rib, so that with the arm adducted the brachial plexus is stretched over the first rib in its altered position.

Repair of nerves in experimental animals

A study of nervous union tissue.—The repair of nerves in experimental animals has been studied by Weiss and Taylor. The lessons from these experiments might help to direct both clinical research and clinical practice. The arterial sleeve-splicing method has many functions in nerve regeneration, including the insurance of straight and unbranched nerve fibre outgrowth and the prevention of the invasion of connective tissue or of fibrotic suture lines. In the authors' experiments, immediately after operation the artery became attached to the nerve endings by clotted blood and lymph; the gap between the nerve ends was filled by blood clot. This clot was so organized in a few days that the severed portion of the nerve became rewoven, thus allowing the transit of sheath cells and regenerating axons from one stump to the other. The tissue which filled the gap and reunited the stumps was called by the authors 'union tissue'. By contrast, the scar between two nerve endings not protected by a sleeve became invaded by connective tissue cells and a sort of block was formed to the continuity of the nerve. The two stumps instead of being an integral fabric over which sheath cells, nerve fibres, blood vessels and capillary liquid passed easily, were patched up by a 'mechanical cementing' of low permeability. The results of control experiments, in which a nerve was merely cut and the two endings just left close together, showed that optimal nerve regeneration was possible only with arterial splicing. Even the luxuriant axon branching which occurred in the control experiments did not equal in any way the perfect result of sleeve-spliced stumps. As for nerve endings which were sutured by thread, the scar here gave a worse result. In arterial splicing the primary part played by the artery is to give full play to the tension mechanism which affects tissue growth in general. Whole blood was an adequate medium for the foundation of a bridge between the cut nerve endings. By the third day the blood clot had become a series of longitudinal pathways for subsequent cell and fibre growth. This transformation in the clot is the result of tension factors arising outside and inside the clot. A major source of deflection was pressure of the two nerve endings against one another. By the combined effect of tension and fibrinolysis the framework of the nerve stumps becomes

rewoven throughout the former gap; the connecting fibrin threads of the clot act as guides for the outgrowing sheath cells and axons.

Repair

Use of preserved cadaver grafts

Klemme, Woolsey and de Rezende describe 3 cases of successful repair of injured peripheral nerves by the use of preserved cadaver grafts. In the past the failure of peripheral nerve surgery was largely due to the formation of scar tissue and neuromas caused by the methods then in vogue. Experiments in animal nerve surgery made at the Yale University School of Medicine Laboratory of Physiology during a period of 2 years, in which the grafts were joined to the cut ends of the nerves by a 'glue' of 50 per cent pure acacia or acacia fortified with vitamin B and B complex instead of by sutures, promised success in the human subject. The first patient, a girl aged 8 years, was operated on in August 1942 for a severed common peroneal nerve which had caused right foot drop and sensory defect. She can now walk with only a slight limp, can tap dance and run easily on both feet. The second case was that of a man of 35 years; after a bullet wound in the left chest he had sensory and motor changes in the left hand and fingers due to a lesion of the ulnar nerve. Operated on in November 1942 he is now beginning to have return of function. The third case, in which repair of an injured ulnar nerve was done in January 1943, is too recent for judgment of result. Post-operative treatment of the patient is important. Splints should not be used but only a simple snugly fitting bandage. Two weeks after operation the application of moist heat to the grafted area is advisable, and gentle massage and motion may be begun. In some cases gentle electrical stimulation was used and appeared to be of value in bringing about more rapid return of function after nerve grafting.

Klemme, R. M., Woolsey, R. D., and de Rezende, N. T. (1943) *J. Amer. med. Ass.*, **123**, 393.

Meadoff, N., and Gray, A. B. (1944) *Physiotherapy Rev.*, **24**, 10.

Weiss, P., and Taylor, C. A. (1943) *Arch. Surg., Chicago*, **47**, 419.

NEURALGIA, GLOSSOPHARYNGEAL AND TRIGEMINAL

See also B.E.M.P., Vol. IX, p. 174.

Trigeminal neuralgia

Aetiology and pathology

Success of surgical treatment.—Krayenbühl reviews the causes and treatment of trigeminal neuralgia. The cases fall into two categories, (1) symptomatic trigeminal neuralgia and (2) idiopathic trigeminal neuralgia. Symptomatic trigeminal neuralgia may result from the following causes: (1) toxic-infective processes in the distribution of the nerve such as dental caries, pyorrhoea and sinusitis or general toxic-infective conditions, including diabetes, alcoholism, syphilis and so forth; (2) intracranial inflammation, tumour or aneurysm involving the nerve roots, ganglion, or central tracts. In these cases other neurological symptoms and signs are usually present, as in a patient described by the author who had a malignant tumour which started in the left antrum and which was associated with trigeminal neuralgia, optic atrophy and almost total ophthalmoplegia on the left side. In idiopathic trigeminal neuralgia obvious cause of pain is not present and other neurological signs and symptoms are absent. It occurs most commonly in women; a series of cases described by the author included 35 women and 18 men. The pain occurs in paroxysms, characteristically brought on by sensory stimuli of different kinds. Surgical treatment gives results so good that other forms of treatment such as alcohol injection are falling more and more into the background. The method favoured by the author is transection, partial or complete, of the sensory root. The mortality is low and the results are excellent. Alternatively the Gasserian ganglion may be coagulated by diathermy, but although in skilled hands brilliant results may be obtained without great risk the method is not considered to be suitable for routine use by all and sundry because of its dangers and uncertainties.

Krayenbühl, H. (1943) *Schweiz. med. Wschr.*, **75**, 1563.

NEURITIS

See also B.E.M.P., Vol. IX, p. 182.

Multiple neuritis

Clinical picture

Similarities to poliomyelitis.—In view of the similarity of clinical findings in acute infective polyn neuritis and in poliomyelitis, Brazier, Watkins and Schwab have studied by electromyography the patterns of electrical activity in the affected muscles of 2 series of 10 patients with these diseases. Comparisons have also been made with patients who have traumatic nerve lesions. Electrical discharges from the affected muscles at rest and during active and passive motion were recorded by an oscillograph. Surface electrodes were usually used but in some cases these were supplemented by coaxial needle electrodes inserted in the belly of the muscle. The following similarities of muscle dysfunction in infective polyn neuritis and poliomyelitis were shown. Muscle tenderness and paresis are characteristic of both diseases, and the electrical abnormalities in both cases are correlated with weakness rather than with

sensitivity. Partially paralysed muscles when stretched show hyperirritability, which can be relieved by hot fomentations. Even at rest paretic muscles are hyperirritable and discharge electrical potentials characteristic of regenerating motor units. Reciprocal innervation is often disrupted in polyneuritis and poliomyelitis, with resultant simultaneous activation of opposing muscles. This abnormality is probably secondary to painful motion. The disorganization of reciprocal innervation is not so severe in polyneuritis as it is in poliomyelitis, for the simultaneous activation of opposing muscles in the former is not characterized by synchronization of component discharges.

Brazier, Mary A. B., Watkins, A. L., and Schwab, R. S. (1944) *New Engl. J. Med.*, **280**, 185.

NEUROSYPHILIS

See also B.E.M.P., Vol. IX, p. 224; and Cumulative Supplement, Key Nos. 1151–1166.

Intracranial syphilis

General paralysis of the insane

Malarial therapy.—Nicole tabulates the results attained in the malarial treatment of neurosyphilis during a period of 20 years. General paralysis affected 90 per cent of the 604 patients concerned of whom 401 were successfully inoculated with malaria, each experiencing an average of 7.9 rigors. Administration by the intramuscular route early superseded that by intravenous and subcutaneous inoculations. Infection produced by mosquito bite was reserved for resistant cases and for the introduction of new strains. Taking the departure rate from hospital, including recoveries, as an index of success the 38 per cent departure rate of malarial cases outstrips the 3 per cent departure rate of cases non-malariously treated. Of 109 recoveries, 83 patients on admission had been bedridden, wet and dirty or affected by seizures. Therefore the indications are that advanced cases are not hopeless. The serological findings were impaired by the inaccessibility to examination of patients cured and discharged. Blood becomes negative less readily than does spinal fluid, which is believed ultimately and usually to return to normal. In Nicole's series the return in the order of numerical results was seen by (1) cell count, (2) protein content, (3) globulin tests, (4) Wassermann tests, (5) Lange tests and (6) Kahn tests. Absolute serological cures exceeding 40 per cent are not claimed by Nicole as it is known that serological relapses, often accompanied by clinical relapse, do occur. Longevity tables showed that of 250 patients treated by malaria therapy 86 survived for 10 years, whereas one only of 125 treated without malaria survived for this period. Other deductions of the author's are, first that repetition of malarial attacks may be beneficial; secondly that drugs, notably but not only tryparsamide, reinforce malarial treatment; finally that malarial treatment although incapable of repairing organic damage does in half the number of cases cure or suppress the advance of neurosyphilis.

Nicole, J. E. (1943) *J. ment. Sci.*, **89**, 381.

NOSE AND NASOPHARYNX DISEASES

See also B.E.M.P., Vol. IX, p. 256; and Cumulative Supplement, Key No. 1168.

Interpretation of symptoms

Functional defects

Rhinoplasty as a remedy.—Wolf emphasizes the functional benefits deriving from the operation of rhinoplasty which formerly aimed at aesthetic effects only. Ideally the main current of air inspired is directed upwards from the inferior turbinate bone over the middle concha, forming whorls and eddies during its passage, and so downwards to the choanae. Correctly to guide this current and to purify it are functions of the vestibulum. Deviation of the current from its proper route may result in anosmia and in liability to colds and to sinusitis. Less directly rhinitis sicca, atrophic rhinitis and frontal headache are traceable to this source. Respiratory anosmia results from deflection of the air current along the floor of the nose; it is amenable to rhinoplasty. Atrophic rhinitis is usually associated with unduly capacious nasal chambers. Narrowing operations, being complicated, are often declined by the patient and the drawbacks of submucous injection of paraffin have led to its abandonment. Here the narrowing effect of rhinoplasty often gives gratifying results and the benefit in rhinitis sicca is even more pronounced. Similarly, certain types of frontal headache of uncertain causation have yielded to rhinoplasty. The anatomical irregularities which especially require correction by this operation are an elongated tip of the nose, asymmetrical and slit-like nostrils, a hypertrophied columella or a nose laterally deviated. When submucous resection or turbinectomy is performed the therapeutic result is often marred by omission of simultaneous rhinoplasty. It is essential to eradicate any purulent or polypoid condition of the sinuses before proceeding to this operation.

Obstruction

Naso-pharyngeal fibroma.—Of tumours of the nasopharynx seen by Tirumal Rao in 15 years at Vizagapatam 22 were malignant and there was one nasal fibroma and the 17 nasopharyngeal fibromas reported on here. Sixteen of Tirumal Rao's patients were males; the manifestation of the growth about the time of puberty and its regression with adolescence were considered to be significant. The fact that the fibroma will regress does not justify delay

in treatment, since choking, sepsis, haemorrhage and cerebral involvement continually threaten disaster. The sphenoid and pterygoid bones, the basilar process and the atlas or axis are common sites of origin. The fibroma is pedunculated or sessile and as it is not encapsulated it forms secondary attachments which invade the retromaxillary fossa, the antrum, the orbit and the cranium. Biopsy is hazardous since the blood vessels are devoid of muscular coat. Round sarcoma-like cells lie between the fibrous bundles but the fibroma does not become sarcomatous. Nevertheless differentiation will lie between fibroma, fibrosarcoma, antrochoanal polypus, fibroma of nasal origin and epithelioma. Obstruction to breathing, epistaxis, nasal discharge, deafness, headache and later vomiting appear. Deglutition becomes embarrassed and respiratory obstruction may require treatment by tracheotomy. At the Mayo Clinic treatment by radiotherapy and surgical diathermy has taken the place of surgical treatment with the result that mortality has decreased and more success has been obtained. At the King George Hospital, Vizagapatam, radiotherapy sometimes supplemented by surgery, has cured 3 out of 10 cases and has given relief to 4 patients. Three cases have been fatal. On one occasion, as radium was not available, injections of monochloroacetic acid gave relief.

Effect of slynasol.—In a preliminary report on a new approach to the treatment of snoring, Strauss laments the neglect with which 'this serio-comic symptom' has been treated in the past and reports 7 cases in which the condition has been dealt with by the injection of a sclerosing fluid, slynasol, into the body of the soft palate, the base of the uvula, and the free edges of the posterior pillars of the fauces. Slynasol is a weak soap consisting of the sodium salts of certain fatty acids extracted from a seed of the psyllium group. Two per cent benzyl alcohol is added for its anaesthetic effect. At a sitting not more than 0.5 cubic centimetre in small divided doses is injected deep into the tissues of the soft palate. Spots of tincture of metaphen or merthiolate are applied at the sites of injection in deference to asepsis. Of the 7 patients one was completely cured, 3 were greatly improved and 3 failed to show benefit by the treatment. Strauss defines snoring as 'a coarse low-pitched noise produced by vibrating soft tissues in the nasopharynx of a sleeping person', and excludes laryngeal stridors, asthmatic wheezing and similar noises; he divides the victims into organic and functional snorers. The former owe their infirmity to adenoids, polyps or tumours, to deflection of the septum or to nasal allergy and for these individuals ordinary standard measures are indicated. The functional snorers are individuals with normal air passages or in whom correction of an abnormality has failed to cure the symptom. For them Strauss advocates the use of sclerosing substances in order to produce fibrosis of the tissues of the vibrating soft palate and faucial pillars, and so prevent their noisy fluttering in the air tunnel in which they are placed.

Strauss, J. F. (1943) *Arch. Otolaryng., Chicago*, **38**, 225.

Tirumal Rao, B. (1944) *J. Indian med. Ass.*, **13**, 95.

Wolf, G. D. (1943) *Amer. J. Surg. N.S.*, **62**, 216.

OESOPHAGUS DISEASES

See also B.E.M.P., Vol. IX, p. 287; and Cumulative Supplement, Key Nos. 1176–1188.

Ulceration: Peptic ulcer of the oesophagus

Clinical picture, diagnosis and treatment

Record of ten cases.—Peptic ulceration of the oesophagus, according to Cleaver, who records 10 cases, is less rare than is supposed. It arises because diaphragmatic hernia and a shortened oesophagus relax the cardiac sphincter and thus regurgitation of the gastric contents is permitted. More rarely there is intrusion of gastric mucosa in the oesophagus. The symptoms are pain, haematemesis and dysphagia. Pain is sternal or epigastric and radiates to shoulders and arms. Haematemesis may be of coffee-ground material or of bright blood. Fatal haemorrhage from aortic erosion is recorded. Dysphagia, initially slight, increases as stricture develops. When oesophagoscopy reveals an ulcer and radiography a diaphragmatic hernia with shortened oesophagus, confirmation is complete. Ulceration varies from the small and round to the large and annular erosion. Its morbid anatomy is identical with that of gastric ulcer. Perforation may occur into pleura, pericardium or bronchus. Infection of the mediastinum is rare. When biopsy shows ectopic gastric mucosa the treatment is the same as that for gastric ulcer. The usual type of peptic ulceration, with shortened oesophagus, requires the ingestion of lukewarm fluids and semi-solids every 3 hours. Belladonna is administered 20 minutes before feeding in doses daily increasing until dry throat or disturbed accommodation occurs, and immediately before feeding a tablespoonful of mineral oil is given. Feeding by duodenal tube with milk, orange juice, liver extract, corn syrup and ascorbic acid is satisfactory and assists in preventing stenosis. The bed head should be raised at night in order to prevent gastric regurgitation. Dysphagia which persists after 3 weeks of treatment requires dilatation by Jackson's bougies. The trend is towards complete healing.

Tumours

Malignant

Review of modern treatment.—Taylor says that there were 1,703 male and 716 female deaths from carcinoma of the oesophagus in 1937. The tumour is of relatively low malignancy. Dysphagia is rather a late symptom, and there should be watchfulness for complaint of

aching or burning pain in the chest or throat associated with a tendency to regurgitation after meals. Oesophagectomy is successful in early cases. Radiotherapy by radium or by X-rays has been disappointing. Among palliative methods, he condemns gastrostomy. Souttar's tube is often satisfactory and the endoscopic insertion of radon seeds may restore the lumen by destroying the centre of the growth. He has experimented with an operation which, if successful, will restore the continuity of the alimentary canal at one stage. It consists in resection of the affected part of the oesophagus with immediate subcutaneous anastomosis outside the thorax. In the discussion on Taylor's paper, Levitt suggested that with careful selection the palliative value of deep X-ray therapy was considerable. Its most important contra-indication was mediastinitis, the two cardinal signs of which condition were substernal pain and persistent tachycardia usually without pyrexia. The best results were in cancer of the upper third of the oesophagus, with growths which showed fat fleshy fungations into the lumen. A judicious combination of X-rays with intracavitary radium might prove worth while. Steele stated that, with Jobson, he had introduced radon seeds through the oesophagoscope in 60 cases and temporarily restored ability to swallow. Lederman stated that the best results yet obtained were those of Guisecz who used a radium bougie; of his 270 cases 11 patients survived for more than 3 years and 12 for over 18 months. The palliative value of the bougie was shown by the rapid relief of symptoms and the avoidance of gastrostomy. The treatment of cardio-oesophageal tumours by laparotomy and insertion of radon seeds was worth trying in an otherwise hopeless case. Harnett quoted statistics published in 1942 by the British Empire Cancer Campaign. Of 470 cases, 205 were treated surgically, 43 by radium and 139 by X-rays. The thorax was explored in 17 cases and oesophagectomy done in 5 of these, all without successful results. Patients treated by implantation of radon seeds and by deep X-rays had their expectation of life increased by 2 months and 3 months, respectively. Smithers had found that X-ray treatment relieved symptoms in many patients and gave an occasional 5-year 'cure'. In carcinoma of the thorax oesophagus, Negus considered the only satisfactory method to be the implantation of radon seeds. It was possible to restore normal swallowing of food and saliva with very little discomfort to the patient although life was not prolonged.

Cleaver, E. E. (1943) *Amer. J. digest. Dis.*, **10**, 319.

Taylor, H., Levitt, W. M., Steele, G. H., Lederman, M., Harnett, W. L.,

Smithers, D. W., and Negus, V. E. (1944) *Proc. R. Soc. Med.*, **37**, 331.

OVARY DISEASES

See also B.E.M.P., Vol. IX, p. 318; Interim Supplement, No. 17*; and Cumulative Supplement, Key Nos. 1191-1196.

Tumours

Clinical types

Brenner tumour.—To 170 cases of Brenner's ovarian tumour hitherto recorded, mostly since 1932, Ayre and Kearns add 3 instances. Macroscopically 2 types of tumour are seen, (1) the solid and (2) the cystic. The epithelial cell nest is characteristic of both and displays undifferentiated pavement epithelium peripherally and mature squamous epithelium centrally, embedded in a fibrous stroma. These squamous cells are large, polyhedral, regular and clear-staining with relatively small oval nuclei. Scattered throughout the cell nest are areas of cystic degeneration around which the epithelial cells assume columnar form. The cystic areas sometimes contain mucoid material and sometimes ovum-like cells, hence Brenner, assuming an ovular origin, designated the tumour *oophoroma folliculare*. This histogenetic theory is now displaced and the tumour is believed to originate in the Walthard rest, an abnormal differentiation of the coelomic epithelium found in ovary, tube and mesosalpinx. Whereas granulosa-cell neoplasms cause temporary sterility, a corpus luteum has been noted in association with Brenner's tumour which is also known to have obstructed labour. This contrasting effect of the two tumours on ovarian activity indicates their different origin. The menopause however has usually preceded operative removal. The tumour is benign and shows neither metastasis nor recurrence after removal. If the tumour is too small to be palpable concomitant pelvic disease alone reveals its presence. Diagnosis is dependent upon the use of the microscope since there are no means by which it can be made clinically.

Bilateral ovarian cyst

Associated masculinization.—Turner describes an example of masculinization associated with bilateral microcystic disease of the ovaries. The patient, a single woman aged 23 years, complained of amenorrhoea and hirsutism of 6 months' duration. She had to shave her chin every few days. The pubic hair was masculine in distribution. Both labia were atrophic, the clitoris 2.5 centimetres long, the uterus very small, the right ovary somewhat enlarged. X-ray examination made after injection of air did not reveal any enlargement of the adrenal glands. Laparotomy showed that both ovaries contained multiple small cysts. Two-thirds of each was resected. Menstruation recommenced and the hirsutism gradually disappeared.

Parasitic ovarian cyst

Four stages of development described.—Kantor describes the development of parasitic ovarian cyst as occurring in 4 stages: (1) slow torsion of the pedicle with gradual cutting off of the blood supply; (2) formation of adhesions to omentum or other structure; (3) secondary vascularization through these adhesions; (4) complete amputation of the pedicle. The case is

reported of a woman aged 30 years who complained of attacks of lower abdominal pain. Exploratory laparotomy disclosed that the right ovary was converted into a multilocular dermoid cyst attached laterally by a pedicle composed of the right infundibulopelvic ligament and amputated right uterine tube, and by a second pedicle to the bladder. Another, smaller, dermoid cyst was embedded extraperitoneally in the right lateral pelvic wall. A third was found attached to the omentum; as the left uterine tube had undergone amputation and no left ovary was found it seemed that this cyst had developed in the left ovary. Menopausal symptoms appeared after the operation.

Ovarian cyst and pregnancy

The main complications.—Three cases of ovarian cyst in pregnant women reported by Capone illustrate some of the complications which may occur, namely rupture, rapid growth and suppuration in the cyst. The first patient, aged 28 years, was delivered with high forceps after a labour lasting 3 days. All went well until the twelfth day when there developed abdominal pain and distension with fever. The leucocyte count on the fourteenth day was 34,600. A tender mass the size of a large orange was felt in the right iliac fossa. The patient was treated with sulphathiazole and blood transfusions until the acute condition had subsided. Laparotomy on the eighteenth day revealed a dermoid cyst of the right ovary with an old rupture. The second patient, aged 19 years, 7 months pregnant, complained of extreme increase in the size of the abdomen and of dyspnoea. She was found to have a very large cyst which, when removed 8 days after a normal delivery at term, contained 14 pints of fluid. The third patient, aged 29 years, was admitted to hospital 7 days after a miscarriage, with pain, fever, a mass in the pelvis and a leucocyte count of 11,800. At operation a suppurating cyst as large as an orange was removed. The author recommends ovariectomy in all cases of ovarian cyst complicating pregnancy, but avoids operation during the first 3 months because of the risk of removing the corpus luteum and causing an abortion. There is a greater chance that complications will occur in pregnant than in non-pregnant women.

Hypernephroma of the ovary

Metastatic spread.—Kannerstein, Brown and Rosen report a case of hypernephroma of the ovary in a 52-year-old woman. She was taken suddenly ill with colic, became collapsed and comatose and died within 30 hours. One kidney had been removed 11 years previously for hypernephroma. Necropsy disclosed that death was due to bleeding from a ruptured ovarian tumour. This consisted of a serous cyst with a hypernephromatous mass embedded in its wall. The histology of the tumour was characteristic. The authors state that only 2, possibly 3, other cases of metastatic hypernephroma of the ovary are recorded.

Clinical picture of all types

Meigs's syndrome.—Meigs, Armstrong and Hamilton report on 2 cases of the syndrome known by the senior author's name, comprising fibroma of the ovary, ascites and hydrothorax. They point out that the clinical picture invites a diagnosis of cancer with metastases and on this account some patients have been denied operative relief. Fluid in the abdomen is a frequent accompaniment of fibroma of the ovary and ceases to be produced after the tumour has been removed. The reason for the production of fluid is unknown and the way in which in some cases it reaches the chest is problematical. In one patient Indian ink injected into the abdomen was subsequently detected in equal concentration in the fluid from the abdominal and thoracic cavities and was not found in the blood. Samples from both cavities were identical in all aspects measured. Passage of particles from chest to abdomen could not be demonstrated.

Differential diagnosis

Histological picture of developmental tumours.—Bhaskara Menon, Veliath and Khanolkar point out that in the embryological development of the ovary there are 3 phases, (1) the indifferent or dysgerminal, (2) the protesticular or masculine and (3) the ovarian or feminine. The tumour, dysgerminoma, is believed to arise from the first phase of gonadal development. The histology shows a resemblance to that of seminoma of the testis. Although these tumours are of rapid growth secondary deposits are rare, so that their histological malignancy is not a true criterion of prognosis. There were 7 cases in this group and the average age was 17 years. Arrhenoblastoma is said to arise in the second phase of development; it may be a persistent remnant of a protesticular phase which usually disappears in the female ovary. Such tumours tend to produce masculinity. Granulosa-cell tumours arising from the third phase of ovarian development have a feminizing effect. According to Khanolkar these tumours may occur at any age and constitute about 3 per cent of all solid ovarian tumours. He also describes lutein-cell tumours, only 12 of which have been recorded in the literature and 3 of which may have been adrenal cortical tumours. Khanolkar also states that theca-cell tumours, genetically related to granulosa-cell tumours, occur, usually after the menopause; they are unilateral and only one case of doubtful malignancy has been described. Brenner tumours are said to arise from a rest of indifferent cells on the ovarian adnexa and one case is described. The authors say that although such cell rests are found on the Fallopian (uterine) tubes and uterine ligaments, yet tumours of Brenner type have not yet been reported in these places. The authors' case showed masses of epithelioid cells and cystic spaces. This histology suggests that the Brenner tumour originates from coelomic epithelium. Surgical removal is the treatment for all these growths; after operation the patient usually is restored to normal health.

One point worth noting is that these tumours are frequently associated with fibroids or with cancer of the uterus.

Ayre, J. E., and Kearns, P. J. (1943) *Canad. med. Ass. J.*, **49**, 404.

Bhaskara Menon, T., Veliath, G. D., and Khanolkar, V. R. (1943) *J. Indian Med. Ass.*, **12**, 337, 343.

Capone, A. J. (1943) *Amer. J. Surg. N.S.*, **61**, 387.

Kannerstein, M., Brown, C. R., and Roscn, J. A. (1943) *Amer. J. Obstet. Gynec.*, **46**, 290.

Kantor, H. I. (1943) *Amer. J. Obstet. Gynec.*, **46**, 412.

Meigs, J. V., Armstrong, S. H., and Hamilton, H. H. (1943) *Amer. J. Obstet. Gynec.*, **46**, 19.

Turner, S. J. (1943) *Amer. J. Obstet. Gynec.*, **46**, 295.

PANCREAS, DISEASES

See also B.E.M.P., Vol. IX, p. 386; and Cumulative Supplement, Key Nos. 1203–1208.

Developmental abnormalities

Annular pancreas

Report of a case.—In all 46 cases of annular pancreas have been recorded. Stofer reports on a further case and draws attention to a careful scrutiny in 7,095 necropsies during 14 years. This produced 3 more cases, an incidence of rather less than 1 in 2,500 necropsies, which indicates more frequent occurrence. The annulus is traversed by and constricts the duodenum. The man described, aged 62 years, was admitted to hospital for recurrent depressive psychosis, and for persistent vomiting during 6 months. Physical examination did not elicit any signs of organic disease, but radiologically a duodenal abnormality, interpreted as a diverticulum, was detected. The fact that similar misinterpretation has been reported twice previously suggests that the finding of duodenal diverticula may indicate annular pancreas more often than it is usually recognized to do. Efforts to improve the patient's condition preparatory to exploration failed, and death ensued. Necropsy showed the annulus, posteriorly and near the head of the pancreas, to be completed by fibrous tissue. The additional tissue which formed the annulus possessed its own duct which injection was unable to connect with the main pancreatic duct. This lack of connexion has been found by another worker. In 12 of the 46 recorded cases other congenital malformations, usually gastro-intestinal, co-existed. Horseshoe kidney and a double hiatus of the diaphragm are also on record. In the author's case the associated malformation assumed the unusual form of cerebral distortion. The convolutions of the cortex were of abnormal pattern and the ventricles were dilated. There were also present a small cavity in the globus pallidus and an adenoma of the pituitary gland. The duodenum showed a ring of constriction between proximal and distal dilatations, and the stomach was dilated.

Inflammatory conditions

Chronic

Assessment of pancreatic function.—Bauman and Whipple investigated the value of pancreatic function tests in 47 surgically treated cases. A special tube is used which is divided into two compartments by a longitudinal partition; one compartment is perforated at what will correspond to the level of the stomach and the other at the duodenal level. Since acidification with hydrochloric acid destroys the pancreatic ferments, separate aspiration of the stomach is necessary in order to avoid this. The tube was passed into the duodenum under X-ray control. Fifteen milligrams of mecholyl were injected subcutaneously and 4 samples at 10-minute intervals were collected from the duodenum in tubes immersed in ice-water. Amylase, protease and lipase contents were estimated. The results are divided by the authors into 2 groups. Normal results were obtained in cases of stone or cancer of the bile-ducts. In tumour of the ampulla normal pancreatic juice may be obtained if the pancreatic duct or ducts enter the duodenum separately or if there is an accessory duct of Santorini. In only one patient with proven cancer of the pancreas were normal ferments obtained; in this case the neoplasm of the head of the gland invaded the common bile-duct without obstructing the pancreatic duct. In the group of normal results pancreatic disease was seen in only one subject, in whom biopsy showed an occasional patch of fibrosis. The second division included all the cases which showed abnormal ferment concentrations due to proven pancreatic disease. The authors state that painless obstructive jaundice, with low or absent pancreatic ferment concentrations, is almost always due to cancer of the pancreas. Functional disturbances of the external secretion of the pancreas may occur without demonstrable histological changes in the gland.

Calculi

Aetiology

Review of pancreatolithiasis.—The increasing frequency of reports on pancreatolithiasis is attributed by Pasternack to the more frequent use of radiography of the abdomen in the diagnosis of digestive disorders. The pancreatic calcification may be in the form of a calculus (or calculi) or of the deposition of calcium salts in the parenchyma itself. The latter is probably the sequel to infection, inflammation or necrosis. Edmondson and Fields found large quantities of calcium in acute pancreatic lesions and observed that the serum calcium in such

conditions fell between the third and the eleventh day of the disease. Chronic disease of the biliary tract is a frequent association with pancreatic calculi. The two forms of calcification may occur separately or concomitantly and in very advanced cases the gland may be transformed into a solid mass. The concretions consist chiefly of the carbonates and phosphates of calcium and are therefore radio-opaque. The physical qualities are very variable, ranging from gravel to very large deposits. Secondary changes of atrophy and fibrosis of the gland may result and obstruction may give rise to cystic masses and to superimposed secondary infection to suppurative processes. The acinar tissues are the first to suffer but when the disease is far advanced the islands of Langerhans are involved. The symptomatology is vague and variable. Pancreatic colic, which may be indistinguishable from biliary colic, has been reported in two-thirds of the number of recorded cases; the mobility of the stone is the influencing factor in this symptom. Jaundice may be present because of incidental disease of the liver or from blocking of the ampulla by a pancreatic calculus. Episodes of acute pancreatic necrosis may occur. Reflex symptoms of digestive upset are common. Changes of the motions indicative of pancreatic insufficiency are seen in about half the number of cases. Latent or active diabetes mellitus is not infrequently present. Diagnosis must depend upon radiological examination; oblique views are necessary to demonstrate the radio-opaque areas. A peculiar feature is the predisposition to pulmonary complications such as tuberculosis, suppuration and gangrene.

Treatment

Description of two cases cured by pancreaticolithotomy.—Lionello, Ficarra and Ryan report on 7 cases of pancreatic calculi, in 2 of which cure was effected by pancreaticolithotomy. The authors consider that faulty diagnosis may be responsible for the apparent rarity of the condition. X-rayfilms are necessary; the stones are radio-opaque because of their large calcium carbonate content. Stagnation of pancreatic juices as a result of chronic infection is the dominant aetiological factor; exfoliation of cells, precipitation of lime salts and formation of calculi result. Pancreatic calculi are to be distinguished from parenchymal calcification but both not seldom co-exist, the latter on a basis of chronic pancreatitis. Fatty degeneration of the liver may result from deficiency of lipocaic. The first case operated on was a man of 56 years of age. The clinical impression was that of cholecystitis with cholelithiasis, but radiography revealed the true state. Under spinal anaesthesia the pancreas was exposed and the head noted to be indurated; 2 stones were found in the pancreatic duct. The calculi were removed with a clamp and the pancreatic incision then sutured with atraumatic catgut. A drain was inserted at the operative site. The second example was a man of 35 years of age who had previously had 4 operations for gastric ulcer. Again an X-ray examination of the abdomen showed calcification and at operation 4 calculi were removed from the pancreatic parenchyma. Both patients made a good recovery. Excoriation of the skin was prevented by the application of a mixture of equal parts of kaolin and olive oil. A low carbohydrate diet was given after the operation. Ephedrine was used in order to reduce the pancreatic juices.

Tumours

Carcinoma of pancreas

Total pancreatectomy.—A case of carcinoma of the pancreas with total pancreatectomy has been described by Rockey, who states that a search of the literature revealed only 2 references to so-called total pancreatectomy. Whipple, Hunt, Brunschwig and others have dealt with methods of removing the head of the pancreas and the duodenum combined with disposition of the flow. In the author's case there was a massive carcinoma of the body of the pancreas together with distinct fibrosis and adhesions although the tail of the pancreas was free. The gall-bladder and the bile-duct were dilated but did not contain any stones. At operation the duodenum was divided at its junction with the jejunum. The common bile-duct was cut and ligated. The tumour was freed with difficulty from the adherent coeliac axis and hepatic artery. The entire pancreas, the lower half of the stomach and the entire duodenum were removed in one piece. Anastomoses were made between jejunum and stomach and between jejunum and fundus of gall-bladder. Post-operative diabetes was controlled by administration of 27 units of insulin daily. Death from peritonitis (bile) occurred 15 days after operation.

Bauman, L., and Whipple, A. O. (1944) *Amer. J. med. Sci.*, **207**, 281.

Lionello, J., Ficarra, B. J., and Ryan, N. H. (1944) *Arch. Surg., Chicago*, **48**, 137.

Pasternack, J. G. (1943) *Ann. intern. Med.*, **19**, 757.

Rockey, E. W. (1943) *Ann. Surg.*, **118**, 603.

Stofer, B. E. (1944) *Amer. J. med. Sci.*, **207**, 430.

PEPTIC ULCER

See also B.E.M.P., Vol. IX, p. 504; and Cumulative Supplement, Key Nos. 1236 and 1237.

Peptic ulcer of stomach and duodenum

Aetiology

Incidence.—Tidy¹ depicts the changes in incidence of peptic ulceration. Acute ulcers, formerly prevalent among young women, disappeared with chlorosis although there is not any evidence that chlorotic girls were prone to peptic ulcer. Chronic gastric ulcer, occurring predominantly in males, increased in incidence and soon the duodenal ulcer became commonplace instead of

rare. The incidence of peptic ulcer increased prodigiously between the wars of 1914–18 and the present war. Its common development in reservist and recruit is due to recrudescence of peace-time ulcers and, since treatment cannot effect a 'cure', discharge becomes a necessity. The causation of peptic ulcer remains obscure. Heredity and excess of free hydrochloric acid are unsatisfactory explanations and although psychological stimuli may pull the trigger—as is shown by the common occurrence of perforations during air-raids—it cannot load the gun. Diagnosis must rely on symptoms, examination, radiography, gastric and faecal analyses and gastroscopy. Hunger pain, punctual in its recurrence, nocturnal, and relieved by food and antacids, characterizes duodenal ulcer. Palpation unless unexpected is frustrated by muscular rigidity. In gastric ulcer the patients dread the pain consequent on eating; the pain is relieved by vomiting but not always by antacids. In both ulcerations radiography, although occasionally deceptive, is often decisive and is a better means of detection than is gastric analysis. Hyperacidity nearly always accompanies duodenal ulcer although it does not prove its presence; in gastric ulcer acidity may approach the normal. Faecal examination for occult blood remains unreliable but gastroscopy in gastric ulcer is advancing in diagnostic value. Essential treatment comprises rest in bed and meals taken initially at two-hour intervals; the diet should be ample and varied and should include two pints of milk and abundant vitamins. Aluminium hydroxide or simple carbonates are preferred as antacids. The use of tobacco, suspected as having a bad effect, should be forbidden at first and later should be restricted. The teeth should always be put in order. Perforation and pyloric obstruction necessitate operation always, recurrent haemorrhage sometimes, although blood transfusion has revolutionized its treatment. Malignancy invades probably 3 per cent of gastric ulcers, but duodenal ulcers never become malignant.

Deficiency of amino-acids and the vitamin B complex.—The cause of peptic ulceration as pictured by Steele is a dietetic deficiency, probably of the amino-acids and the vitamin B complex. This deficiency produces hepatic degeneration which leads to faulty tissue metabolism. Thence arise those areas of lowered resistance in the gastric and duodenal mucosa which are peculiarly susceptible to the action of hydrochloric acid. This theory embraces the neurogenic theory of causation, since hyperchlorhydria and gastric motility are notably fostered by an oversensitive nervous system which may be traced back to faulty tissue metabolism in the brain substance. The similarity of response to identical treatment suggests the relation between allergy and the ulcerous diathesis. Distension after meals, sudden fatigue, headache and ophthalmic discomfort—symptoms common to both conditions—indicate the added presence of cholecystitis, for which bile-salts are the most efficient chologogue. Other medicinal measures which are advocated include vitamin saturation and the administration of an iron salt and of liver extract given orally or sometimes by intramuscular injection. A light carbohydrate diet, a diminution of fats and fried foods and a low meat allowance are prescribed. When the diagnosis of ulceration is established by physical signs, X-rays or gastroscopy, the recognized treatment for ulcer must supersede treatment for cholecystitis; but the restricted life and the imminence of operation which confront the patient with manifest ulceration call for prophylactic measures.

Influence of the emotions.—According to Wolff gastro-duodenal ulceration is correlated to the influence of the emotions on the motility and acidity of the stomach. It had been found that emotions experimentally induced resulted in a rise in acidity and in increased contractions of the stomach and confirmation of the findings is given by Wolff's report on the effect of natural emotions. The patient was a subject dependent upon a surgical gastric fistula; his oesophagus became occluded in childhood when he swallowed a quantity of scalding fluid. A collar of gastric mucosa protruding from the stoma showed during emotional quiescence 3 small rhythmic contractile waves in each minute. Every 3 hours a phase of hyperaemia, acidity and peristalsis ensued which lasted for 20 minutes. During 34 observations it was possible to identify a dominant emotion of contentment, joy, dejection, fear or hostility. Fear and dejection produced pallor of the mucosa with diminished acidity, motility and response to food. Anxiety and hostility produced hyperaemia with increased acidity and motility although the period of normally accentuated function was due to occur 90 minutes later. Prolonged gastric activity was observed during a fortnight of financial anxiety. During such activity the mucosa was unduly susceptible to the production of erosions by trivial injury. These erosions healed readily under a protective and neutralizing layer of mucus. Similarly, irritants such as acids or mustard applied over a coating of mucus had little effect but their application to an area kept denuded caused inflammation and oedema. It is inferred that the hyperaemia of emotional states with its concomitant hyperacidity persistently acting on minute erosions is the prelude to peptic ulceration.

Pathology and morbid anatomy

Statistics of six necropsies on young children.—Benner reports 6 cases of peptic ulcer discovered during about 500 routine necropsies on young children. One infant, aged 2 days, showed early pneumonia, otitis media and a duodenal ulcer with pronounced inflammatory changes and no evidence of repair. Another child, 3 days old, had a malformation of the heart and extensive ulceration of the duodenum. The history given was of failure to retain food or water from the time of birth. In this case the appearances suggested that spontaneous submucous haemorrhage had preceded the ulceration. The third child, a boy of 14 months old,

had tuberculous meningitis and a superficial duodenal ulcer with moderate leucocyte infiltration. Another, aged 11 years, with a duodenal ulcer 1 centimetre in diameter, died of meningitis secondary to otitis media. It is suggested that the disease of the central nervous system may have been a factor in the production of the ulcer in these 2 cases. The fifth child, aged 3 years, had been poisoned by eating rhubarb leaves and had a very large duodenal ulcer presenting the appearances typical of chronic ulcer in adults in a state of acute exacerbation. The author suggests that a pre-existing chronic ulcer was activated by the poison. In a child of 10 years of age with appendicitis and pneumonia, small multiple gastric ulcers were found. In 2 other children, aged 2 months and 9 years respectively, scars which appeared to be due to healed ulcers were found in the duodenum. The author comments on the absence, with one exception, of a history suggestive of gastro-intestinal disease.

Clinical picture

Preponderance of duodenal lesions.—Kirk reports the findings in a group of patients with peptic ulcer who were admitted to the gastro-intestinal section of a military hospital. During the 5-month period under review 385 patients entered the section and of these 50 (12·9 per cent) had radiologically confirmed ulcers, 49 being duodenal and only one gastric. Most of the patients were between 20 and 30 years old at the onset of symptoms, the oldest being only 36. Cases with symptoms of under 12 months' duration, 14 in all, were classified as acute; in 11 the symptoms had appeared after a length of service sufficient to allow them to be regarded as the result of it. Correlation was not observed to exist between the gastric acidity and the severity of the symptoms; 10 patients in the series had not any free hydrochloric acid. The most constant symptom was intolerance to greasy foods, of which 88 per cent of the men complained. The pain was characterized by an occurrence late at night and a tendency to radiate to the back. No relation was noted between ulcer and psychoneurotic manifestations; the theory of an emotional basis for peptic ulceration was unsupported also by the results of treatment, since most patients made a prompt response.

Course and prognosis

Massive haemorrhages in six members of a family.—Boros describes a family in which the mother and 5 of her 11 children had massive haemorrhage (haematemesis or melaena or both) from peptic ulcer, as had the daughter of the eldest son. The mother died at the age of 86 years from uncontrollable gastric ulcer bleeding. A son aged 47 years had a large haemorrhage from a duodenal ulcer. Another son aged 54 years also had a severe haemorrhage from a duodenal ulcer. A third son aged 53 years had several bleedings from a duodenal ulcer and, despite a gastro-enterostomy and later a subtotal gastrectomy, had further massive bleedings. A fourth son, who had been suffering from a duodenal ulcer for over 25 years, died from massive ulcer haemorrhage at the age of 63 years. A daughter aged 63 years had had ulcer symptoms for many years and had been treated by gastric resection. None the less she had a massive haemorrhage from a duodenal ulcer. The daughter of the eldest son, aged 45 years, had had a subtotal gastrectomy at the age of 37 years; later, she had 4 severe bleedings, and a jejunal ulcer has developed. There were 5 sons and one daughter (of the first patient considered) who were quite free from ulcer symptoms. The failure of operative treatment in this family is emphasized and it is suggested that operative treatment may have to be applied with caution if there is found to be a familial tendency to peptic ulcer.

Mortality statistics.—Tidy² reports the trends of the crude death rates for peptic ulcer in Great Britain from 1912 to 1938. Striking changes have taken place during the last 20 years of this period. The data are from the annual reviews of the Registrars-General and the annual reports of the London County Council. Between 1912 and 1920 there was not any appreciable rise in the death rates for peptic ulcer. Between 1921 and 1930 there was a rapid rise but from 1930 to 1938 there was not any significant further rise. The greatest rise was between 1921 and 1925. The only exception to these findings was in males in Scotland over 40 years of age suffering from gastric ulcer. The rise in the death rates was maintained. The rises are almost confined to patients over 40 years of age. As regards sex incidence, the rates for females, both over and under 40 years of age, have not shown any real tendency to rise, whereas gastric ulcer in females under 40 has fallen steeply in continuation of a decrease which began in previous decades. The rise in death rates for peptic ulcer in the population has been due almost entirely to that in males over 40 years. The death rate for gastric ulcer throughout this period is much in excess of that for duodenal ulcer for both sexes and age groups and all areas—except for males in Scotland after 1927. Death rates in England from gastric ulcer showed a slow rise up to 1938 in males over 40 years of age. For duodenal ulcer the rate became nearly stationary after 1930 in all age groups and sex groups and in all areas. Death rates for peptic ulcer are highest for London, slightly lower for Scotland, lower for England, and lowest for the rural districts of England. In Scotland the trend of the rates for gastric ulcer in males over 40 years of age is entirely different from that in England. In rural districts the rates for males over 20 years of age are about 60 per cent of those for London and for Scotland, and 80 per cent of those for England.

Differential diagnosis

Main points in radiological diagnosis.—Borman describes 7 cases of active ulceration in the upper part of the descending duodenum—a very infrequent location and one in which the radiological diagnosis is seldom made. From the radiologist's point of view the differential diagnosis offers four possibilities. (1) Simple diverticula are usually easily recognized. Their

chief features are smooth rounded shape, presence of mucosal folds in the stalk, mobility and absence of tenderness, size (averaging 3 centimetres in diameter), multiplicity, absence of spasm or distortion of mucosal pattern in the adjacent duodenum. Inflammatory traction diverticula offer greater difficulty in recognition and radiologically cannot always be distinguished from acute ulceration. Multiplicity is the most important characteristic. Solitary pseudo-diverticulum secondary to healed ulceration of the cap may simulate an ulcer of the descending duodenum, but the deformity is usually limited to the cap and does not produce secondary changes in the descending duodenum, such as are often found to be present in cases of ulcer. (2) Cancer—an extremely rare lesion of the duodenum—tends to encircle the bowel and to obliterate the mucosal folds. (3) Filling of the ampulla of Vater may occur in association with chronic pancreatitis. It is very rare and transient, the barium being rapidly evacuated. (4) Primary duodenitis may be indistinguishable from acute ulceration or from the residual changes which ensue after healing. Absence of localization is the most important sign. Radiologically ulcer of this region tends to produce a filling defect, due to invagination of the ulcer bed by scar tissue, rather than a crater or a niche. The lesion is usually situated on the outer and posterior margin of the bowel. In all the cases here reported on, however, the upper and inner margin was involved and a crater was present. Secondary spasm, mucosal distortion and medial retraction of the adjacent upper descending duodenum were present in every case. Clinically these ulcers are often associated with severe bleeding.

Gastroscopy.—Poor illumination, rigidity disposing to perforation or inability to train a flexible instrument on the target handicapped the early use of gastroscopy. Gill describes the passage of Hermon Taylor's instrument and the information afforded in research and diagnosis. The patient, who has fasted for 6 hours, receives a $\frac{1}{4}$ -grain of morphine hypodermically one hour before the introduction of the instrument and 20 minutes before it he dissolves a tablet of anethaine in the mouth. Occasionally general anaesthesia is required in addition; pyloric obstruction necessitates aspiration of the gastric contents. The patient lies on the left side with hips flexed. The operator draws the epiglottis forward with the left index finger and gently passes the lubricated flexible tip down the oesophagus, countering any resistance with patience, not pressure. The normal orange-red mucosa blanches during fear and flushes when in excitement or when secretion is induced. To radiography, especially if negative or inconclusive, gastroscopy is complementary. In the author's series of gastric ulcers 17 per cent eluded X-ray diagnosis. The erosions believed to presage peptic ulcer are rarely detected radiologically. In suspected cancer, disproof by means of gastroscopy may save exploratory laparotomy; confirmation will prevent delay in operating. The gradations of gastritis—superficial and curable, or hypertrophic and atrophic demanding permanently adjusted diet—are differentiated by gastroscopy. After haemorrhage gastroscopy, delayed as safety dictates, is informative. Its findings may decide between gastro-jejunostomy and partial gastrectomy or determine a patient's readiness for discharge. The contra-indications are laryngeal infections, oesophageal lesions, aortic aneurysm and pyrexial or debilitating illness. Kyphoscoliosis or spinal rigidity prove to be an anatomical bar. The important complications are oesophageal inflammation, which usually yields to treatment with sulphathiazole but occasionally advances to an abscess requiring drainage, and, very rarely, perforation at the cardiac orifice which necessitates laparotomy.

Treatment

Prophylaxis with enterogastrone.—Ivy suggests the possibility of affording protection against recurrent peptic ulcer by intramuscular injection of an extract of duodenal mucosa containing enterogastrone. Since fat acting on the intestine and certain pyrogen-free extracts of intestinal mucosa administered parenterally inhibit gastric secretion and motility, a principle common to both was postulated, denominated enterogastrone. Later, extracts were prepared inhibiting secretion only and further a body termed urogastrone, possibly representing excreted enterogastrone, was recovered from the urine. Urogastrone although identical with enterogastrone in action is indifferent to pepsin, which renders enterogastrone inert. The complexity of enterogastrone is thus established. In the author's experiments a non-irritant form of enterogastrone was extracted and 112 dogs were prepared for the experiment by means of gastro-jejunostomy, as the result of which there was a diversion of the bile and pancreatic juice to the extremity of the ileum. Of the dogs not receiving enterogastrone, 98 per cent succumbed to ulcer within 9 months. Of 25 receiving enterogastrone intramuscularly 6 (25 per cent) developed ulcers, 8 died of extraneous causes and 11 survived without developing ulcers. On the cessation of treatment after one year, only one of the 11 developed ulceration 18 months later. Subcutaneous injection gave similar results. The mechanism of the increased resistance to ulceration remains uncertain since a significant depression of gastric and pepsin secretions was not proved. Studies by other investigators suggest that enterogastrone promotes mucosal repair. Fifteen patients with a history of recurrent peptic ulcer were treated with the same preparation of enterogastrone and palliative results were obtained, but insufficient time has elapsed to justify a claim for immunization from recurrent ulcer. The effects of alcohol, tobacco and caffeine on the stomach are considered to consist in the predisposition of the gastric mucosa and glands to ulceration. Alcohol, which is irritant and acid-promoting, is condemned by the author; smoking is considered to be detrimental but, inasmuch as its ill effects are inconsistent with gastric findings, they are attributed to indirect cardio-vascular effects. Any dose of caffeine exceeding 72 milligrams stimulates gastric

secretion. The synergy of alcohol and caffeine concomitantly ingested intensifies their potency as gastric stimulants.

Drugs successful during fasting hours.—King, Comfort and Osterberg report on the volume and hydrogen ion concentration of the gastric and duodenal contents in 3 normal fasting persons before and after the administration of certain drugs tested by the continuous aspiration method with removable sample-collection receptacles. Some observations were made in which the gastric and duodenal contents were aspirated simultaneously but separately; others were made in which the gastric contents were allowed to enter the duodenum and the mixed gastric and duodenal contents were then aspirated. The drugs were administered by injection. Atropine sulphate ($\frac{1}{100}$ grain) reduced both the amount of acid secreted and that entering the duodenum and also the buffering value of the duodenal contents. The result of its action is a greater average hydrogen ion concentration of mixed duodenal and gastric contents. Morphine sulphate ($\frac{1}{8}$ grain) reduced the volume of the contents of the stomach and of the duodenum promptly and notably. These drugs usually caused bile to disappear completely from duodenal contents within 20 minutes and to remain absent for over 3 hours. Administration during the tests of glyceryl trinitrate (nitroglycerin) and amyl nitrite did not reduce the time during which bile was not to be found in the duodenal contents. The sodium salt of dehydrocholic acid (sodium dehydrocholate) (10 cubic centimetres of a 20 per cent solution given intravenously) seemed to be capable of provoking a flow of bile great enough to raise slightly the hydrogen ion concentration of the fasting gastric and duodenal contents, as aspirated already mixed. Secretin (one clinical unit per kilogram of body weight given intravenously) provoked a secretion of pancreatic juice sufficient to raise and maintain the mean hydrogen ion concentration at higher levels than did other drugs. These results show that atropine sulphate, the sodium salt of dehydrocholic acid and secretin are rational in the treatment of peptic ulcer at least during the fasting hours. In the case of the last two drugs, however, the intravenous route, the possible reactions and the cost limit their practical use. The authors' results indicate that the clinical value of bile salts would be small.

Post-operative gastric acidity.—Heuer and Holman have made determinations of the pre-operative and post-operative acidities in 163 patients with peptic ulcer who underwent either gastro-enterostomy or gastric resection. The results show that 37.4 per cent have achlorhydria or low acidity whereas 62.6 per cent have an adequate or high acidity. The clinical results however were satisfactory in 83.4 per cent of these patients. It would appear therefore that the beneficial results of the operations are not necessarily due to decreased acid secretion. In a series of 75 patients after gastro-enterostomy there was not any notable change in acid secretion yet clinically 75 per cent of this series were satisfactory in a post-operative period which covered 10 years. The authors find that after gastric resection there is usually a reduced secretion of acid depending upon the extent of the operation, although gastric resection of reasonable size does not ensure achlorhydria. It is probable that here too dilution and neutralization of acid are important factors in obtaining good results. It may thus be better not to make large gastric resections in the hope of ensuring achlorhydria but rather to make smaller resections which should give fair results and would also allow a further operation in case of recurrence of the ulcer. These findings do not deny the cause and effect of acid and ulcer. The authors state that it is possible that operations other than gastric resection may achieve a more constant reduction of acid.

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PERITONITIS: ACUTE PERITONITIS

See also B.E.M.P., Vol. IX, p. 537; and Cumulative Supplement, Key No. 1241.

Treatment

Effect of sulphonamides

In the United States of America 20,000 deaths occur annually from peritonitis due to perforation of the appendix, according to Stafford, Beswick and Deeb. Between 1929 and 1939 fluid infusion, gastro-intestinal decompression and improving technique were assisting to reduce this total. In order to assess the additional benefit of sulphonamide medication, 903 operations which were performed during the period 1939 to 1942 are analysed. Appendectomy was performed in 789 cases and there were 114 instances of simple incision and drainage. During 1939 sulphonamides were administered parenterally to 12 per cent of cases

and the mortality rate was 9·2 per cent. During 1940 the intraperitoneal introduction of sulphonamides, alone or occasionally combined with parenteral administration, was employed in 58 per cent of cases and mortality fell to 7·1 per cent. Combined administration, which is growing in favour, was employed in 98 per cent of cases in 1942 and the mortality was then 3·4 per cent. During 1939 appendicectomy was performed in a quarter of the number of abscess cases with a 21 per cent mortality. By 1942 sulphonamide treatment had warranted an increase to three-quarters of the number—without mortality. Concurrently great decrease was shown in pulmonary involvement, metastatic abscess and the need for peritoneal drainage. The method of parenteral introduction preferred by the authors is the intravenous administration of 2 grammes of sulphathiazole in 5 per cent solution every 8 hours for 10 doses; administration is begun 24 hours after operation. For intraperitoneal use crystals are preferred to powder. Ten grammes of sulphathiazole crystals are implanted and a further 2 grammes are sprinkled in the abdominal wound. The possibility of permanent hepatic damage was kept in mind but not any evidence of it was found although there was transient jaundice in 3 cases.

Stafford, C. E., Beswick, J., and Deeb, P. H. (1944) *Amer. J. Surg. N.S.*, **64**, 227.

PHARMACOLOGY

See also Interim Supplement, Nos. 12*, 15* and 20*.

Administration of drugs

Sublingual administration

Walton has investigated the value of drugs when administered sublingually. In order to be certain that a drug is not effective by sublingual administration, doses considerably larger than the minimally effective subcutaneous dose must be given. In the course of his experiments Walton found that the penetration of drugs through the oral mucosa was a strictly selective process. The most important determining factor is the fat-water distribution coefficient; the penetrability of drugs may be predicted by this physico-chemical constant. Organic nitrates have a relatively high solubility in fats and their efficacy by sublingual administration has been amply proved. Coefficients of approximately 20 to 30 are on the borderline of effectiveness. Steroids and androgens have been prescribed sublingually with satisfactory results. Oestrogens were similarly potent by this route. Recently desoxycorticosterone acetate has been shown to be of value by the sublingual or sublabial route in the treatment of Addison's disease. Apomorphine shows a high rate of absorption through the oral mucosa. The conclusion reached concerning morphine derivatives was that these compounds cannot be given sublingually with good effects. Similar negative results were obtained with ergot, atropine, mecholin (acetyl- β -methylcholine chloride), strychnine, picrotoxin and barbiturates. Cardiac glycosides were also ineffective. In the mouth, conditions of competition of solvents prevail, the predominant competition being between the aqueous salivary fluids and the fat in the protoplasm of the cells. The author suggests that 'the most feasible method of improving the sublingual penetrability' of drugs is by means of 'the preparation of chemical derivatives with more favourable solubility characteristics'.

Anti-bacterial agents

Effect of oestrogens

Faulkner deals with part of an investigation which is attractive as a new line of research, namely an attempt to discover if substances which are known to have physiological effects on animal metabolism have any recognizable action either on bacterial growth and reproduction or on the simple chemical reactions characteristic of the metabolism of bacteria. Preliminary trials showed that stilboestrol possesses some degree of bactericidal activity. As it appeared possible that this fact might be put to some chemotherapeutic use the subject was investigated further. Subsequently other substances with oestrogenic properties were examined for any correlation between the oestrogenic and the bactericidal activities. Of the oestrogens produced in the animal body oestradiol and oestrone were investigated and of the synthetic oestrogens in addition to stilboestrol, hexoestrol and diethoxytriphenylbromoethylene. Hexoestrol gave results similar to those given by stilboestrol but the naturally occurring oestrogens and diethoxytriphenylbromoethylene were not found to inhibit any of the organisms tested. The substances were used sometimes in the form of tablets or ampoules as marketed for clinical use and sometimes as pure crystals. The conclusions reached were that stilboestrol is bactericidal, and in less concentrations bacteriostatic, to Gram positive cocci, *Corynebacterium diphtheriae* and *Neisseria catarrhalis*; that no inhibitory action on the Gram negative cocci was found; that the minimal lethal concentration varies somewhat between the organisms but that in all those recorded it lies between 1 in 5,000 and 1 in 500,000. Tubercle bacilli were killed by incubation *in vitro* by the action of stilboestrol 1 in 5,000 but its bactericidal power is reduced in the presence of serum.

Antiseptics

Organic detergents

Tests with phemeride.—Certain compounds, known as organic detergents or wetting agents, have the power to lower the surface tension of solutions which contain them and to enable the solution to make intimate contact with—or to wet—surfaces which otherwise would not

be affected in this way. According to Iland the mode of action on bacteria, although undetermined as yet, probably is to disrupt and interfere with the functions of the bacterial cell membrane; it has already been shown that various substances which lower surface tension can penetrate and disperse mixed lipo-protein layers and that this power can be related to their lytic activity on red blood corpuscles, unicellular animals and bacteria. So far these organic detergents have been employed, not on account of their antiseptic powers, but simply because they have the ability to increase the potency of other antiseptics when mixed and used with them. Attention has now been drawn to the use of certain of them as antiseptics. Iland records tests made on phemeride (*para-tertiary-octylphenyldiethoxybenzylidimethylammonium chloride*), a new quaternary ammonium compound of this type. He describes *in vitro* tests made for the purpose of assessing its bacteriostatic power in broth and blood, its anti-leucocytic and bactericidal actions and its effect on emigration and phagocytosis. Clinical tests made in order to ascertain its action in infected areas such as thoracic wounds and fistulae and its sterilizing and possible irritant action on the skin are described and although no definite conclusions could be drawn from the small number of tests done the author considers that phemeride merits further study since it appears to be inhibitory to common pathogens in dilutions which are not toxic to the tissues. If, in addition, it has synergistic properties, better chemotherapeutic preparations for infected wounds and body cavities may become possible.

Chemotherapy

Mechanism of chemotherapeutic action

In a discussion of kationic chemotherapy Albert first outlines the mechanism of chemotherapeutic action, using sulphanilamide in illustration. The metabolism of every cell and bacterium centres in the enzyme systems, combined with a chemical body. Chemotherapeutic attack concentrates on enzyme systems which are vital to bacterial metabolism but relatively unimportant to the host. The chemical body which is essential to most bacteria is *p*-aminobenzoic acid; it is so closely allied to sulphanilamide that when sulphanilamide is administered the enzyme accepts the substitution. The trifling difference in the new enzyme combination renders it, nevertheless, unserviceable to the bacterium. Its metabolism and reproduction cease and it yields readily to the defence forces of the body. Such is the general mechanism of pharmacological action. The kationics employed are generally hydrochlorides or sulphates of bases which have high molecular weight, form neutral solutions in water and are often highly coloured. The kation or base of the antiseptic apparently combines with an anion, probably nucleic acid, of the bacterium. Although only complementary to the sulphonamides, the kationics possess certain superiorities over other antiseptics with the exception of penicillin. They are unaffected by *p*-aminobenzoic acid, which is abundant in pus and renders sulphonamides inert. They are active against organisms which have become sulphonamide-fast and they excel against *Clostridium welchii*. On the other hand the use of the acridine compounds as powders in fresh wounds must not be allowed and the frothing kationics are neutralized by soap. The frothing kationics—zephiran, Ctab. and phemoral—reduce the surface tension of water; they rapidly sterilize intact skin or instruments and cleanse dirty wounds. They are unsuitable for repeated application. Of the acridines crystal (gentian) violet is efficient in burns and propamidine when Gram negative strains are absent. Acriflavine, which is toxic, is obsolescent. Proflavine and 5-aminoacridine are outstandingly successful in gross sepsis, in the prophylaxis of gas gangrene and in brain surgery. The official proflavine sulphate is somewhat acid. By the addition of one quarter of its weight of sodium bicarbonate, a neutral non-irritant preparation is obtained.

Review of forty years' progress.—In the Frederick Price Lecture delivered to the Royal College of Physicians, Edinburgh, Dale contrasts the lack of therapeutic resources 40 years ago with the present state of affairs. Then the scope of medicinal treatment was usually limited to the relief of symptoms. For malaria, amoebic dysentery and syphilis specifics were known although their use was still almost wholly empirical; the treatment of myxoedema and cretinism with thyroid gland and of diphtheria with antitoxin had already begun. The lecturer recalled the treatment of diabetes without insulin, of pernicious anaemia without liver, of rickets without vitamin D. The greatest advances however are seen in the field of synthetic chemistry, where Ehrlich was a pioneer. He led the search for artificial remedies which would act directly on the causes of infection and it was he who coined the word, chemotherapy. The discovery that the benzidine dye, trypan red, could overcome trypanosome infection in mice and in rats was the starting point for a whole series of discoveries. Ehrlich's theory that the parasite was not killed but was rendered incapable of reproduction received confirmation some years later from studies of the action of emetine upon *Entamoeba histolytica* in which this mode of action was demonstrated. Another important line of research originated in the discovery by Thomas and Breinl that atoxyl (*p*-aminophenylarsonic acid), an organic derivative of arsenic acid, cured trypanosome infection in small rodents and the discovery has led to the introduction of the various arsenicals for syphilis. The action of these compounds may, it is suggested, be owing to the deposition of the drug within or upon the bodies of the spirochaetes and the steady production from it of arsenic in lethal concentration. The discovery by Domagk that prontosil, now termed prontosil rubrum (4-sulphonamido-2': 4'-diaminoazobenzene), was effective in mice infected with streptococci marked another new departure. Evidence has been obtained that the action of some chemical compounds upon pathogenic

organisms is not to kill them outright but so to interfere with their vital processes as to starve them gradually. This concept, first advanced by von Jancsó to explain (quite erroneously) the action of synthalin (decamethylene-guanidine) upon spirochaetes, has been revived in connexion with the sulphonamides. It has been found that these are inactivated by the presence of *p*-aminobenzoic acid, which is present in streptococci and is closely allied to sulphanilamide in chemical structure; the suggestion has been made that the effect of sulphanilamide depends upon its capacity to preoccupy some cellular enzyme which normally acts upon *p*-aminobenzoic acid. The discovery of penicillin opens another new chapter in therapeutics.

Acridine

Discussion of derivatives

Drug fastness or drug resistance of bacteria is an increasingly widespread phenomenon, only to be overcome by an increase in the variety of chemotherapeutic agents, supplemented perhaps by acridine antiseptics. Martin tabulates 53 derivatives of the parent substance acridine, the antiseptic potency of which is correlated with basicity. The acridines are excreted in bile and urine. Acridine readily forms azo complexes such as sulphonamido-azo-acridinium, and these may prove valuable in chemotherapy. Proflavine (2 : 8-diaminoacridine sulphate) and acriflavine are chosen for detailed consideration. Users of acridine derivatives differ widely in their findings. These discrepancies are probably proportionate to the purity of the preparations used. In the treatment of superficial wounds, whether or not flavines are efficiently bactericidal in concentrations harmless to leucocytes and fibroblasts, is controversial. One school of observers wholly condemns the flavines, whereas reports from the North African campaign are wholly favourable—80 cases treated without failure. They found that proflavine was less toxic than acriflavine and that up to 2 grammes placed in the wound succeeded, especially in staphylococcal infections, in which all other medicaments failed. In systemic therapeutics unmodified acridines, excepting 5-aminoacridine hydrochloride and 2 : 7-diaminoacridine hydrochloride, are probably unsuitable. The subcutaneous injection of acriflavine, used in gonorrhoea, although therapeutically effective, was too painful for out-patient use. Among organisms reported susceptible to acriflavine are trypanosomes, staphylococci, *Bacillus coli*, streptococci and the organisms of anthrax and cholera. Among organisms unaffected by acriflavine are those of malaria, tetanus, typhus fever and tuberculosis and the *B. pyocyaneus*. The gas bacillus is reported unaffected by some observers, but others have found the *Clostridia welchii*, *Cl. oedematiens* and *Cl. septicum* susceptible to proflavine, especially if combined with sulphathiazole. In gonorrhoea the oral administration of 0.1 gramme (1½ grains) of acriflavine has proved an efficient urinary antiseptic, and the acridines may prove valuable in sulphonamide-resistant gonorrhoea. Success has been attained in meningococcal meningitis. Toxic hepatitis has occurred after excessive doses of acriflavine, but within therapeutic limits the danger is considered negligible.

Amphetamine

Experiments with benzedrine on dogs

Alpern, Finkelstein and Gantt performed experiments on dogs for the purpose of discovering the effects of amphetamine (benzedrine) sulphate administration upon nervous activities. The quantitative determination of conditioned reflexes was used as an accurate index of cerebral functioning. The conditioned salivary reflex gave an estimation of secretory activity, the leg withdrawal reflex to a conditioned stimulus (a bell) was an indication of motor activity, cardiac and respiratory rates measured autonomic reactions, and finally, the effect of the drug upon sexual activities was reflected by the period of erection, duration of erection and latent period of ejaculation to a constant, unconditioned sexual stimulus. The quantity of conditioned parotid secretion was found to be but little altered by a strong excitatory stimulus, to be moderately increased by a weak excitatory stimulus and to be slightly increased by an inhibitory stimulus. The latent period was decreased. The incidence of foot withdrawals was decreased to an excitatory stimulus and increased to an inhibitory stimulus. The conditioned changes in respiratory and cardiac rates also showed a loss of differentiation. With regard to sexual activity, it was noted that there was a diminution in intensity soon after the compound had been given. The authors conclude that the chief effect of amphetamine (benzedrine) sulphate on the higher nervous activities was a moderate loss of differentiation in all the conditioned reflexes employed. Since the giving of benzedrine increased the conditioned secretion relative to the unconditioned secretory responses, it was thus an excitatory stimulant of the supra-segmental nervous system. The possible inhibition of at least part of the segmental nervous system was demonstrated by the reduction of the unconditioned secretion to food and unconditioned sexual reflexes. Thus, 3 effects of benzedrine on the nervous system in dogs appear and since each effect may be dominant under various conditions a possible explanation is afforded for variability in response to the substance in man.

Arsphenamine

Late type of hepatitis

Beattie and Marshall emphasize that there are apparently two types of hepatitis which occur during arsenical therapy: (1) an early type which is usually mild and appears within the first 2 weeks after the first injection of the drug and (2) a late type which may appear at a variable time after starting treatment but usually between the twelfth and seventeenth weeks of treatment. The authors are concerned with the late type. They quote Goodman and Gilman

who stated that jaundice during arsphenamine treatment is due in many cases to 'non-specific catarrhal jaundice, occurring in patients whose livers are subjected to the added insults of syphilis and an arsenical'. Beattie and Marshall produce evidence to show that there are two distinct diseases giving jaundice which cannot be differentiated clinically and biochemically. They call infective hepatitis 'X disease'. This has an incubation period of about 30 days and is transmitted by contact. It may exist in a form in which icterus never appears, but which nevertheless confers immunity against reinfection. Late post-arsphenamine jaundice and homologous-serum jaundice is called 'Y disease'. This has an incubation period of about 90 days and is transmitted by inoculation of infective material such as blood, serum or plasma. An attack of Y disease confers no immunity against X disease. Evidence that an attack of X disease confers no immunity against Y disease is scanty and incomplete, yet is suggestive. So-called relapses of Y disease have been explained as an infection with X disease. It is not known whether an attack of Y disease, due to inoculation with icterogenic serum or plasma, confers immunity against the Y disease which occurs during arsphenamine treatment for syphilis. In view of the identity of clinical, biochemical and pathological pictures of X and Y diseases the final proof of the reality of two infective factors is still awaited.

Cardiac tonics

Digitalis

Administration in different cardiac diseases.—The old practice of prescribing digitalis indiscriminately for every type of heart disease having been shown by Mackenzie to be thoroughly unscientific, was followed by a tendency to restrict its use to cases of auricular fibrillation, until several authorities pointed out that this drug was helpful in patients with congestive heart failure with normal rhythm. Lyon records the results of administering digitalis, either in massive doses or by the ordinary slow method, to 135 cardiac patients of all ages from 6 to 82 years and with various types of disease such as valvular disease, chronic myocarditis and angina pectoris. All showed sinus rhythm but not all showed evidence of marked heart failure. Lyon found that pulse slowing, proportionate to the rate of the heart at the time when the drug was begun, was produced in 90 per cent of 180 trials and that clinical improvement may occur even when there is little or no effect on the pulse rate. He also found that tachycardia and oedema do not necessarily run parallel and that pulse slowing occurred equally readily in oedematous and non-oedematous cases. The total number of cases was insufficient to warrant a detailed analysis of the reactions of the different types of cardiac disorder but the author noted that a satisfactory response was obtained in most cases of chronic myocarditis, that cases of syphilitic origin did not respond as well as did non-syphilitic and that tachycardia was slowed in young individuals who had recently recovered from an attack of acute rheumatism. Furthermore, the giving of massive doses of digitalis to 22 patients with healthy hearts and thereby producing an average slowing of 12 beats, provided additional evidence to refute the assertion that this drug has no action, and therefore no beneficial effect, in cases other than those with auricular fibrillation or gross heart failure with normal rhythm.

Cetyl trimethyl ammonium bromide (Ctab.)

Further experiments with cetavlon

Williams and Clayton-Cooper continue their report on cetavlon (Ctab., cetyl trimethyl ammonium bromide) with Faulkner and Thomas. It was desired to determine whether or not cetavlon reduces the incidence of infection and whether or not healing was delayed. Alternate patients who had small cuts on hand or forearm were selected for experiment and for control. In control patients the surrounding skin was washed with soap and water; in test cases it was washed with 1 per cent cetavlon which, after anaesthetization had been produced, was applied also to the wound. Wounds were treated by excision and suture. Bacteriological studies were confined to the *Staphylococcus aureus*, *Streptococcus pyogenes* and coliform organisms. Swabs taken from the wound before cleansing and at each redressing, and from the skin and air passages, together with the tissues excised at operation, were cultivated aerobically and anaerobically. In preventing infection by the organisms considered cetavlon is estimated to possess an advantage of 17.5 per cent over soap and water. Delay in healing as assessed by contrasting aseptic cases, controls and patients treated with cetavlon, was not observed. Some nurses washed their hands twice daily in 1 per cent cetavlon, and it was shown by means of the patch test that skin sensitivity did not develop. The necessity of two applications is emphasized: the first as a detergent to infected cutaneous debris, the second for antiseptic action.

dl-β-phenyl-n-propylmethylamine

Its use as a vasoconstrictor

Warren, Marsh, Thompson, Shelton and Becker have synthesized a series of aryl-ethylbutylamine, aryl-propylbutylamine and aryl-butylamine compounds in an attempt to produce a volatile amine which would prove to be an efficient vasoconstrictor with relatively little toxic action or stimulating effect on the central nervous system. Among the substances studied *dl-β-phenyl-n-propylmethylamine* appeared to be the most satisfactory, and its pharmacological and toxic reactions were investigated and were compared with those of *l*-ephedrine and with amphetamine, a primary amine. The toxic effects which *dl-β-phenyl-n-propylmethylamine* produced in rabbits, both in acute reactions and after prolonged administration, were

observed. They proved to be similar to those caused by *l*-ephedrine and by *dl*- β -phenylisopropylamine (amphetamine). Lethal doses gave rise to tremors and convulsions and ultimately to cardiac and respiratory failure; sublethal doses resulted in less severe symptoms with an increase in the pulse and respiratory rates. After a prolonged course of administration the blood pressure rose and the pulse rate became slower. Vasoconstriction of the peripheral vessels was noted, and the results in general were approximately the same as those produced by amphetamine. The respiratory rate was increased after administration of *dl*- β -phenyl-*n*-propylmethylamine in normal unanaesthetized dogs; in dogs which had also received an intravenous injection of sodium pentothal the rate was slightly decreased but there was very little change in the oxygen intake. The compound induced bronchial dilatation equal in degree to that produced by amphetamine. *dl*- β -phenyl-*n*-propylmethylamine differed from amphetamine however in that it was much less toxic and caused very little, if any, central stimulation. *l*-ephedrine resembled amphetamine in that it also produced central nervous stimulation although to a lesser degree. *dl*- β -phenyl-*n*-propylmethylamine may prove to be of clinical value in the treatment of nasal congestion arising from various causes.

Demerol

Liability to addiction

Himmelsbach recommends that measures should be taken in order to prevent the abuse of demerol (pethidine hydrochloride) when it is used as a substitute for opium derivatives. The physical dependence action of morphine persists twice as long as does its analgesic action. The two actions in the case of demerol are nearly co-terminous and therefore its liability to produce physical dependence should be less if it is legitimately used. Demerol lavishly administered is known to produce strong physical dependence. It was desired to test whether similar danger pertains to its clinical employment assuming dosage to range from 75 milligrams 4 times daily to 100 milligrams 8 times daily and experiments were performed on groups of former drug addicts. One group received subcutaneously 75 milligrams 4 times daily for 3 months. Subjectively, pleasant effects which lasted for one hour were reported; the effects waned after the first month. Objectively there was little departure from normality. Signs of abstinence such as yawning, lacrimation and dilated pupils followed interruption of administration on the thirtieth and on the sixtieth day. The symptoms were mild and the subjects disclaimed habit formation, professing only a mild predilection. A second group who received 75 or 100 milligrams 8 times daily displayed greater effects and nervousness, irritability and twitching of the muscles were noted. Somnolence and dry mouth during the first week were complained of. Although the symptoms were more intense than those in the first group they were generally mild—four patients showing moderate discomfort—on withdrawal of the drug. The good and evil potentialities of demerol are less than those of morphine but the difference is of degree, not of kind.

Depropanex

Kirwin, Lowsley and Menning investigated the effect of depropanex (deproteinized pancreatic tissue extract) in relieving renal and ureteral pain and in facilitating the passage of calculi. Insulin is known sometimes to cause a fall in blood pressure, because it has a property antagonistic to adrenalin. This property is inherent not in insulin but in the pancreatic extracts containing insulin. Extracts have been prepared which retain the depressor element but are insulin-free, of which depropanex is one. One depressor unit produces a fall in arterial pressure equivalent to the rise produced by 0.01 milligram of adrenalin. Depropanex is standardized to contain 10 depressor units per cubic centimetre. Although it appears to act on smooth muscle, it does not produce the blurred vision and dry throat found after atropine medication and, as contrasted with morphine, it leaves the cerebral centres unaffected. Twenty patients with calculi capable of spontaneous expulsion were studied. The usual dose, injected intramuscularly, was 3 cubic centimetres every 3 hours for 4 doses. Five patients, who were unrelieved, had to be given morphine. Twelve patients experienced relief sufficiently complete to dispense with other analgesia. In 3 cases it was impossible definitely to assign the slight relief to depropanex, nor could cases of expulsion of a stone be so assigned. Eleven patients came to operation. A second study concerned 33 patients who received 3 cubic centimetres of depropanex and 34 who did not receive analgesics, preparatory to cystoscopy with retrograde pyelography. Manipulation was painless in 22 depropanex recipients and 9 controls. Severe pain was experienced by 5 depropanex recipients and 6 controls. For mild or moderate pain the figures were 6 and 19. Depropanex undoubtedly relaxes ureteral spasm.

The diamidine compounds

Stilbamidine

Devine describes experiments made between 1937 and 1941 on the properties and quantitative estimation of the aromatic diamidine derivative, stilbamidine, which seemed to promise well in the treatment of kala-azar and of trypanosome and other infections. It was found that a dilute aqueous solution of stilbamidine, when warmed with glyoxal and an alkali, yielded coloured derivatives. The colorimetric determination could be applied to the study of various properties of the compound. It was found that stilbamidine in aqueous solution is quickly unstable on exposure to light—the stronger the light the more rapid the deterioration; in the solid state the effect of light is less powerful. The trypanocidal activity of an exposed solution

was not found to differ greatly *in vitro* from that of a fresh solution, but the former was found in experiments on mice to become noticeably and increasingly toxic. Stilbamidine is readily adsorbed by various common materials such as charcoal, kaolin and cellulose. It was also assayed spectrophotometrically by means of its absorption peak at 328 m μ , and comparable results were obtained on light-exposed solutions with those obtained colorimetrically. On account of the adsorption properties and restricted solubility of stilbamidine it was difficult to prepare a protein-free filtrate from blood on which to carry out a colorimetric assay. The usual anticoagulants, oxalate and citrate, precipitate the compound and the only blood-deproteinizing reagent found to be satisfactory was dialysed iron, which avoids pronounced changes in hydrogen ion concentration. When exposed to light stilbamidine is as unstable in serum or plasma as it is in aqueous solution.

Diaminosulphone

In experimental tuberculosis

Feldman, Hinshaw and Moses studied the effects of 4 : 4'-diaminodiphenylsulphone (diaminosulphone) on experimental tuberculosis in guinea-pigs. The use of the substance was suggested by earlier work with promin. Three sets of experiments were carried out. In one of them the animals were inoculated with tubercle bacilli 6 weeks before treatment was started and the experiment was terminated 228 days after infection. In the other two the administration of the drug was started 2 days before the infective agent was introduced and the experiment terminated 60 days after infection. The daily dose of the drug was 150 milligrams incorporated with the feed. In such dosage only moderate toxic effects were seen on the blood. Although favourable effects were observed in the two latter experiments, more complete and convincing results were witnessed in the longer experiment which continued for 228 days. In this long-term group the mortality rate was 28.6 per cent as against 71.4 per cent in the untreated control series. Of considerable importance were the necropsy findings. The character and extent of the treated and untreated groups showed great differences; those which had received the drug were without demonstrable lesions or had residual foci in the liver, spleen or lungs in which the process was arrested, calcified or healed. The authors conclude that the results of their experiments indicate that 4 : 4'-diaminodiphenylsulphone is an effective agent in inhibiting or combating experimental tuberculosis in guinea-pigs; the continuous prolonged administration yields cumulative benefits which are not obtained in the short-term experiments and the drug, in the dosage employed, does not appear to be excessively toxic for guinea-pigs. It is emphasized that efforts to obtain a compound more suitable for clinical application should be encouraged.

Dicoumarin

Clinical uses

The administration of heparin is elaborate and costly, and Wasserman and Stats have investigated the comparative anticoagulant value of dicoumarin (dicumarol) (3 : 3'-methylene-bis-(4-hydroxycoumarin)) which is orally administered and inexpensive. Subjects to the number of 71 were selected including 49 patients whose illness—pulmonary embolism, thrombophlebitis, and peripheral arterial disease—called for anticoagulants. In all patients the coagulation time and prothrombin activity were determined. Variability in individual reactions forbade standardization of dosage. Generally, a first administration of 300 milligrams for patients weighing under 130 pounds was adopted and 400 milligrams for those weighing over 160 pounds. Subsequent doses depended with regard to number of administrations and to amount, upon daily anticoagulation and prothrombin tests. A prothrombin index below 50 per cent contra-indicated administration. The latent period, up to 72 hours, and the time required to estimate dosage by the reaction may necessitate the preliminary use of heparin in emergencies. Haemorrhage, not arrested by blood transfusion, constitutes the toxic danger. Operative procedures on the day of first administration are unaffected owing to the delayed action of dicoumarin but the dangers of secondary haemorrhage limit its surgical value. Instances are known of embolism and thrombosis even during periods when the prothrombin index was lowered by dicoumarin. Vitamin K corrects the reduction of prothrombin produced by hepatic disease but does not do so when it is produced by dicoumarin, although this finding has since been modified elsewhere. The pharmacological effect is proved but observation covering 3 months of 10 cases of peripheral arterial disease was rewarded with only one minor alleviation. The therapeutic value is not yet established.

In obstetrics

Davis and Porter describe the results of an investigation into the possible value in obstetrics of dicoumarin (3 : 3'-methylene-bis-(4-hydroxycoumarin)), which is the anticoagulant principle of spoiled sweet clover, the eating of which causes haemorrhagic disease in cattle. In 43 cases of post-partum thrombosis 300 milligrams a day were given in 3 separate 8-hourly doses. This dosage caused no ill effects and appeared to be reasonably safe. The margin of safety is however narrow and it is essential to control the treatment by means of the daily estimation by a skilled technician of the prothrombin, bleeding or clotting time. Overdosage has been found experimentally to produce multiple haemorrhages and both in animals and the human subject individual idiosyncrasy occurs. The cases treated with dicoumarin varied greatly in severity but all showed noticeable improvement in comparison with an equal number of untreated cases. There was some relief of pain, fairly rapid diminution of oedema and a shortened average stay in hospital—19 as against 28 days. Davis and Porter suggest

that the freedom from haemorrhagic complications in their cases may be due to the normal increase in the coagulability of the blood in the puerperium, as other observers have so often reported serious accidents in the treatment of otherwise similar conditions. The authors emphasize the need for great care in the use of this drug.

Oral administration of dicumarol

Dicumarol (dicoumarin), a synthetic anticoagulant, has been used orally with favourable results in 18 cases of different types which are reported by Zucker. Nine of the patients had thrombophlebitis of the legs, two had post-operative pulmonary infarction and one had cavernous sinus thrombosis. None of the patients treated by dicumarol showed any evidence of renal or hepatic impairment. Each adult patient was given by mouth 300 milligrams of dicumarol as an initial dose; subsequent daily doses were usually 200 milligrams, and treatment was controlled by daily estimations of the plasma prothrombin level and by the results of blood and of urine examinations. Other appropriate treatment was given when necessary. Three patients were resistant to the drug; 3 proved highly susceptible to its action. In one patient a transient petechial purpura developed and in 4 other patients slight haematuria, but there was no further evidence of any toxic effect. All the patients recovered; in the patients with thrombophlebitis the pain was reduced or absent when adequate hypoprothrombin-aemia was obtained, and recovery was rapid. In Zucker's opinion dicumarol should not replace heparin administration in emergency cases which require anticoagulant treatment, but it is a cheap and easily administered drug which may prove to be of use in prophylaxis in thrombotic conditions and in embolism, and in treatment of thrombophlebitis.

Dicumarol in thrombosis

The advantages of anticoagulant dicumarol (dicoumarin) therapy in thrombotic emergencies including post-operative venous thrombosis and pulmonary embolism, are discussed by Evans. Dicumarol is the active principle of spoiled sweet clover. He, however, points out the risk of haemorrhage and death with the use of this potent agent. The author has found that it has no consistent effect on the blood cell count or on haemoglobin. The clotting time is prolonged only when the prothrombin time is reduced to about 40 per cent of normal. An initial dose of 300 milligrams for a patient below 120 pounds' weight and 400 milligrams for 1 over 120 pounds' weight is given. A daily dose of 100 to 300 milligrams for 8 days is given, in order to maintain the prothrombin time below 75 per cent. Heparin administration does not affect this dosage. The dosage of heparin is judged by the clotting time. With dicumarol and heparin therapy a patient was able to get up 9 days after a pulmonary embolism. Anticoagulation therapy also greatly shortens the morbidity period in phlegmasia alba dolens. Dicumarol must not be given when there is liver damage or in the presence of a haemorrhagic diathesis. The morning prothrombin time must be determined before the daily maintenance dose is prescribed. Heparin dosage must be controlled by the determination of blood coagulation time, made twice daily.

Magnesium sulphate

Use in cardiac conditions

The value of magnesium sulphate in cardiac conditions is explored by Boyd and Scherf on the basis of an experience recorded by Zwillinger in 1935. Injections were given to 11 patients. One, who had an auricular flutter, was not benefited. Of the remaining 10 patients the majority had organic heart disease; 8 had paroxysmal auricular tachycardia and 2 paroxysmal ventricular tachycardia. To these, in 19 paroxysms, intravenous injections of magnesium sulphate were administered, which ranged from 10 cubic centimetres of a 10 per cent solution to 20 cubic centimetres of a 20 per cent solution. The weaker percentage in small volume was ineffective, but when the volume was increased to 20 cubic centimetres success was attained in 3 out of 9 attacks. When the concentration was increased to 20 per cent in 20 cubic centimetres, success attended each of 8 administrations; this is the dosage recommended. The effect, although occasionally graduated, begins immediately, as it did in 6 patients, or fails entirely, as it did in 4 of the 10 patients. Thirty seconds should be allotted to the injection. Untoward effects were not encountered but one fatality has been reported elsewhere after injection of 30 cubic centimetres of a 25 per cent concentration. Advanced myocardial degeneration, gallop rhythm or pronounced disturbance of intraventricular conduction contra-indicate this treatment. Ordinarily, but for a very short time, magnesium sulphate abolishes the extrasystoles resulting from digitalis in excess, but paradoxically is itself capable of producing extrasystoles; this phenomenon was thrice observed. Stimulation of the vagal reflex through the carotid sinus, Valsalva's experiment or some other procedure affords relief in many cases and should be the first resource. Recourse to injection of quinidine and mecholyl is not without disadvantage and a place may well be found for magnesium sulphate.

Mercupurin

Fatal effects of intravenous injection

Wexler and Ellis report 2 fatal reactions to the intravenous injection of mercupurin. They state that non-fatal reactions of varying degrees of severity are not uncommon. In the fatal cases there is a fall in blood pressure, cardiac upset, cyanosis, dyspnoea, unconsciousness and sometimes convulsions. There are immediate non-fatal reactions in some cases such as occurred in the authors' 2 cases in which the later injections produced a fatal reaction. Post-mortem examination did not reveal the cause of death. The authors suggest that the fatal and the immediate non-fatal reactions may result from the toxic effect of mercury on the heart and

are not anaphylactic. The delayed non-fatal reactions may be due to the diuretic action of the drug. Reactions occur even in patients who are fairly healthy as well as in those who are seriously ill, and in any type of cardiac or renal disease. The ordinary drugs used in heart failure, such as digitalis or nitrites, have no effect on the toxicity of mercurial diuretics. There seems to be no means of preventing fatal reactions. The occurrence of any reaction in a patient requires an immediate revision of treatment. It is pointed out that fatal reactions are rare and that up to date no fatalities have been reported after intramuscular injection of a mercurial diuretic.

Nasal drugs

Comparison of drops, sprays and inhalers

Butler and Ivy conducted an experimental comparison between the efficacy of nasal drops, sprays and inhalers. The results of tests made on human subjects indicate that the nasal sprays and inhalers are more efficient for the application of vasoconstrictor drugs to the normal nose than are nasal drops, and they advocate the former methods in therapeutics. Volatile inhalers and sprays are similar in the intensity and duration of the effects produced. The effects of repeated administration of inhalers and sprays are also similar; both cause far less extensive and serious pathological changes than those which result from the use of nasal drops. Sprays and inhalers are accordingly the methods of choice in nasal medication, but when local areas such as the ostium of a paranasal sinus are treated drops may be preferable. In conditions requiring prolonged and repeated medication nasal drops should be used with great caution; sprays or inhalers are much less likely to have deleterious effects. Griesman discusses the correct mode of administration of oily nasal sprays. He employed various types of oil individually mixed in varying proportions with iodized poppy-seed oil, which produces roentgenographic visibility. He was thus able to trace the distribution of the oils when they were sprayed intranasally. Thirty-one patients of very different age groups were selected, all of whom were free of upper respiratory tract infection. The position of the head was varied and noted. It was found that healthy people irrespective of age might aspirate oil when it was sprayed intranasally even in therapeutic dosage, if it was improperly administered. The presence or absence of tonsils and adenoids does not seem to affect the results. The use before the administration of oil of a 1 per cent solution of an ephedrine salt apparently does not increase the danger of oil aspiration. Scarring of the tonsillar beds and injury to the posterior pillars of the fauces after tonsillectomy tend to increase the danger of aspiration of oil if it is incorrectly administered. As oil is carried downward by the force of gravity the decisive factor of safety or of danger is the position in which the head is held during and after the administration of oil. There is not any danger when the head is held straight or is bent forward, even when massive doses many times the normal therapeutic dosage are employed, and safety increases with the size of the angle of the forward inclination of the head.

Penicillin

Administration

The best route of administration, the optimum dosage and the efficacy of penicillin in various infections are largely, at present, unsolved problems. Bloomfield, Rantz and Kirby report on investigations carried out with the object of obtaining more precise data on these subjects. The inconvenience caused both to patient and staff by the standard procedure of injecting the drug every 3 hours day and night was overcome by instituting either an intravenous or a subcutaneous continuous drip method of administration. The method also had the effect—whether advantageous or otherwise is as yet undetermined—of maintaining a steady concentration of penicillin in the blood stream. The only toxic effects observed were occasional violent febrile reactions or painful sites of injection, both due probably to impurities in the drug. Much difficulty was encountered in evaluating the effect of penicillin in staphylococcal infections, since relapses occurred even after long intervals. Fresh lesions were however decidedly more amenable to treatment than were chronic lesions. The authors concluded that such cases required from 200,000 to 400,000 units per day and that intravenous administration was the most effective procedure. Gonococcal infections on the other hand were usually cured in a day or so by a total dose of from 60,000 to 100,000 units, no matter which method of injection was employed. With many exceptions haemolytic streptococci appeared to be controlled more easily than were staphylococci but less easily than were gonococci. Earlier reports of the rapid disappearance of *Spirochaeta pallida* from surface lesions and the resolution of early lesions under penicillin therapy were confirmed. The drug was also found to be highly effective when injected into closed cavities such as empyema, but quite inactive when instilled into chronic osteomyelitic sinuses. Emphasis is laid on the desirability of team work and of a daily planning of dosage and routes of administration, whenever penicillin is used in a hospital unit.

Antibacterial properties

The antibacterial properties of crude penicillin and their possible clinical applications are described in detail by Fisher. Penicillin is unstable at room temperature but when neutralized and frozen can be stored for some weeks with its activity unimpaired. The potency of penicillin on organisms *in vitro* is similar to that shown in tissue infections, and therefore its bacteriostatic action may be determined by tests on cultures in liquid media. Penicillin is mainly active against streptococci but also it affects gonococci, meningococci, *Clostridium welchii*,

anaerobic streptococci and staphylococci. In Fisher's studies about 13 per cent of the staphylococci were resistant to the action of penicillin; *Escherichia coli*, *Proteus*, *Pseudomonas pyocyaneus* and strains of *Cl. welchii*, *Haemophilus influenzae*, *Eberthella typhosa* and *Salmonella suipestifer* were also resistant. In weak solutions penicillin is bacteriostatic within 5 or 10 hours, and stronger solutions are bactericidal. Crude penicillin is non-toxic to animals, even when used in large quantities; it does not appear to cause hypersensitivity or local irritation (except when used intranasally) or to inhibit the growth of tissue cells. Its bactericidal action on micro-organisms which are resistant to the sulphonamides will probably be of clinical value in the local treatment of certain infections by pyogenic cocci, anaerobic streptococci, gonococci and meningococci and in carriers of meningococci. Trials have already been made in ear, nose and throat infections with encouraging results.

Review of its properties

In a Discussion on the use of penicillin Fleming reviewed the history and characteristics of the crude extract and the more recently prepared active principle which has been obtained by concentration and purification. Penicillin should be used only in cases in which the infecting organism is sensitive to the drug; it is necessary to make estimations of the amount of the compound which is circulating in the blood in order to ensure an adequate bacteriostatic level. Florey described the use of highly purified preparations of penicillin which are bacteriostatic for staphylococci and for streptococci in dilutions of 1 in 50,000,000 and 1 in 100,000,000. The organisms the growth of which is most easily inhibited by penicillin are the gonococcus, meningococcus, streptococcus, pneumococcus and staphylococcus, anthrax bacillus and clostridia. The coliform group, as well as *Bacillus proteus*, *Bacillus pyocyaneus* and the tubercle bacillus are insensitive to the drug. In cases of septicaemia due to infection by organisms in the former group failure with penicillin treatment is due to inadequate dosage, to the use of an inactive extract, or to the insensitivity of the organism, which can acquire resistance to penicillin. Bodenham described successful results in some cases of localized infection which were treated by direct applications of penicillin used in the form of the calcium salt. Three preparations have been used for different types of wounds, namely (1) an aqueous solution, (2) an emulsion cream and (3) a dry powder containing also sulphanilamide and light magnesium oxide. Cutler referred to the value of penicillin in preventing the spread of infection from wounds contaminated by clostridia. The requisite dosage in such cases, however, has not yet been standardized. He described 3 cases in which the use of penicillin did not prevent gas gangrene. Hudson reported that in a series of 33 cases the intramuscular route of administration gave the best results. The combined use of novocain (procaine hydrochloride) and penicillin reduced the irritation caused by the injection without detracting from the success of the results. Christie commented on the method of drip administration into the bone-marrow which has been used with some success. Robinson reported on the results of penicillin treatment in 95 cases of gonorrhoea resistant to the sulphonamide compounds; 94 of the patients were considered to have been cured. In nearly all the cases smears and cultures were negative the day after treatment had been started, although in some cases a urethral discharge persisted for an average period of 3 days. There were not any toxic reactions.

Concentration in the blood

In order to get a successful result with the systemic administration of penicillin, Morgan, Christie and Roxburgh state that there must be an adequate concentration of penicillin in the blood maintained either by continuous drip or by injection; neither method is wholly satisfactory. In some of the authors' cases thrombophlebitis developed during intravenous drip transfusion and was probably due to some impurity in the penicillin. Thirty thousand units of sodium penicillin were dissolved in 1 pint of fluid and were transfused in 6 hours. Damaged renal function may cause penicillin to be retained in the blood stream so that smaller maintenance doses are required. Calcium penicillin was given intravenously in one case with no ill effects. With continuous intravenous transfusions an adequate blood titre can be maintained and the method may also be combined with parenteral fluid administration. On the other hand, thrombophlebitis may often occur and the insertion of a cannula into the vein (for the sodium penicillin solution) prevents the use of the vein on future occasions. With intermittent intramuscular injections 15,000 units were given 3-hourly. The method of administration is simple but it is painful and disturbing to the patient and the rise and fall of blood titre may be a disadvantage. Drip transfusion into bone marrow is of doubtful value except in the case of infants. In continuous intramuscular drip transfusions, the same dose was given as when the intravenous route was employed. This method is almost painless; numerous sites are available for transfusion and an adequate blood titre is maintained. There is however frequent abscess formation and the total fluid intake of the patient may have to be limited.

Effect on bactericidal power of blood and serum

A study of the action of penicillin against *Streptococcus haemolyticus* and *Staphylococcus aureus* in human defibrinated blood and in serum has been carried out by Rammelkamp and Keefer. (1) With haemolytic streptococci the following experiments were made. (a) Known amounts of penicillin were added *in vitro* to whole blood. The various concentrations desired were made by dilution with the same blood. From each dilution an aliquot sample was removed and the serum was separated by centrifuging. The various dilutions of blood and of serum

were used as media for the bactericidal tests. Results showed that the addition of penicillin even in small amounts considerably increased the bactericidal power of both blood and serum and especially of the latter. The maximum effect was obtained with a concentration of 0.03 to 0.3 Florey (Oxford) unit per cubic centimetre of whole blood. (b) Numerous experiments were performed with the blood and serum of normal subjects to whom penicillin had previously been administered by various routes. In every case increased bactericidal power of the blood was noted. Compared with sulphadiazine penicillin showed much greater activity in a concentration of 0.007 Florey unit per cubic centimetre of serum than did sulphadiazine in a concentration of 5.1 milligrams per 100 cubic centimetres of blood. A blood concentration of at least 0.019 Florey unit of penicillin should be maintained when treating streptococcal infections; this requires doses of from 10,000 to 20,000 units given intramuscularly or intravenously every 3 or 4 hours. (2) With 5 strains of *Staph. aureus* similar tests were carried out. When added to whole blood penicillin greatly increased its bactericidal properties. The antistaphylococcal effect of the serum was somewhat less than that of the whole blood. When administered to normal subjects penicillin similarly raised the bactericidal power of the blood. For maximum effect a concentration of at least 0.156 Florey unit per cubic centimetre was required. Penicillin proved considerably more effective than did sulphadiazine. In general staphylococci were less susceptible to penicillin than were streptococci.

Initial clinical trials

The initial clinical trials of penicillin are described by Florey. Laboratory work had previously given the following information: (1) which micro-organisms were sensitive to the drug; (2) that dosage was not likely to be influenced by any toxic effect; (3) that oral administration would be ineffective because of the inactivation produced by the gastric juice; (4) that frequent administration would be necessary because of the rapid excretion of penicillin by the kidneys; (5) that the common antiseptics should not be used at the same time in treating wounds because of the inactivation of penicillin by heavy metals and by oxidation. The earliest trials were made on 200 patients with various local and generalized infections. The results were as follows: complete recovery 143, improvement 43, little or no response 14. These results are the more striking because most of the patients treated during the first year or two had failed to respond to any other treatment, and either were considered moribund or had been ill for months or years. There are two points to be noted. (1) In general infections the temperature never falls rapidly and often rises at first. Regular bacteriological examination is the best means of assessing progress. (2) In local infections the best index of progress is the clinical condition.

Extensive clinical trials

Kecser, Blake, Marshall, Lockwood and Wood report on 500 cases treated with penicillin. Treatment was confined to cases of staphylococcal septicaemia, to staphylococcal, streptococcal, pneumococcal and gonococcal infections resisting sulphonamides and to empyema, meningitis and subacute infective endocarditis. Penicillin was administered intravenously, intramuscularly and topically, including injection into serous cavities. Its rapid excretion necessitates continuous administration or administration every 3 hours. In order to cause active infection to disappear the total average requirement of penicillin is from 500,000 to 1,000,000 Oxford units preferably given over a period of a fortnight or longer. Saline or dextrose solution was the solvent used. For each intravenous injection 1,000 units per cubic centimetre is a suitable concentration. For continuous intravenous infusion, the concentration, in order to produce the dosage desired in 24 hours, was varied and the delivery was regulated between 75 and 100 cubic centimetres per hour. For intramuscular injection a concentration of 5,000 units per cubic centimetre of isotonic solution of sodium chloride should be given in diminishing volume in order to minimize local discomfort. There were many variations in the interval of time which elapsed between the giving of one injection and another, in the total amount of each individual dose and in the total duration of treatment. Staphylococcal infections with septicaemia showed a recovery rate of 54 per cent. Patients under 40 years of age with a site of infection capable of drainage do best. Least auspicious are the cases of patients over 40 years of age who have associated disease. Staphylococcal infections without septicaemia, including osteomyelitis, empyema, infections of skin and subcutaneous tissues and burns, showed a recovery rate of 80 per cent. In the 4 cases of non-haemolytic streptococcal infection penicillin failed to have effect. Of haemolytic infections, 13 out of 23 patients yielded to treatment. Thirty-five of 42 patients with pneumonia recovered, as did 7 of 21 patients with pneumococcal meningitis. Results in pneumococcal endocarditis were disappointing. Although only 4 deaths occurred among the 17 patients with subacute infective endocarditis 10 failed to respond. Since the meningococcus is rarely resistant to sulphonamides, only 5 infections were treated; 4 were cured. The certainty of cure in gonococcal infections is almost absolute. Severe toxic reactions were not encountered.

Need of control in application

Garrod¹ describes penicillin as a therapeutic substance of almost unimagined properties. In anticipation of the time when it will be generally available, he gives a warning that successful treatment with it is not nearly as easy as is treatment with sulphonamides. It has been used so far only under research conditions by experts with the aid of strict laboratory control. Before starting treatment with penicillin it is necessary to determine the nature of the organism and

its sensitivity to the drug. Subsequently, local treatment should be controlled by frequent further cultures, general treatment by repeated estimations of the penicillin content of the blood. Because of the extraordinary instability of penicillin and its liability to contamination with resistant bacteria, it should be dispensed with the greatest care. Penicillin is an unstable acid and the preparations used therapeutically are its salts. The potency, which is expressed in Florey (Oxford) units, varies with the purity of the preparation employed. Although the potency of pure penicillin would be at least 1,000 units per milligram, preparations having a potency of 100 units or less per milligram have given satisfactory results. Whether its effect is bactericidal or bacteriostatic is not clear. This effect is exerted as well in serum, blood or pus as in a simple medium such as broth, but only on certain species of bacteria, mostly Gram positive and including the staphylococcus, pneumococcus, *Streptococcus pyogenes*, the gas gangrene group, *Bacillus anthracis* and *Corynebacterium diphtheriae*. The only fully susceptible Gram negative species are the gonococcus and meningococcus.

Laboratory control

An interim report is made by Garrod² on the laboratory control of penicillin treatment. He points out that penicillin is a labile substance, and also that there are many strains of bacteria which are not only resistant to the penicillin solution but also may decompose it. Before treatment the type of infection should be known. Fleming's agar cup method offers a rapid diagnosis of the responsible pathogen. Occasionally *Staphylococcus aureus* may be penicillin-resistant but *Streptococcus pyogenes*, *Pneumococcus* and *Strep. viridans* were not found to be resistant; *Strep. faecalis* was highly resistant. In mouth bacteria, the mixed and mostly anaerobic infections are generally penicillin-sensitive. The sensitivity of *Actinomyces* varies. In mixed infections the resistant bacteria are usually Gram negative and may produce penicillinase and thus destroy the penicillin in the wound. For the purpose of checking results of treatment swabs are taken from the lesion and are then cultured. Penicillin treatment has not been of any value in cases with extensive bone involvement. An adequate concentration of penicillin in the lesion is necessary for success; the concentration can be tested by determining the penicillin content of the pus. During systemic treatment the penicillin content of the blood should be estimated. This is done by determining the bacteriostatic power of the serum either for the patient's own organism or for a standard staphylococcus.

In infected burns and surface wounds

Advantages over the sulphonamides.—In a paper on infected burns and surface wounds Bodenham deals with their contamination and infection, preventive treatment before reaching hospital and management thereafter. In 75 out of a large number of cases with complete destruction or loss of skin penicillin was used with success after treatment with sulphonamides had been tried with little effect. Penicillin was found to be more active than were the sulphonamides against streptococci and staphylococci, and for removal of sulphonamide-resistant strains of haemolytic streptococci. It does not affect *Bacillus proteus*, or, in concentrations lethal to Gram positive cocci, *B. pyocyaneus*. Penicillin was used, diluted to a standard potency, either in a powder diluted with powdered sulphanilamide mixed with 5 per cent light magnesium oxide, and giving a strength of 1,000 Oxford units per gramme, or in a cream base of equal parts of soft paraffin, lanette wax SX and water, and giving a strength of 100 units per gramme. Both preparations were easily sterilizable. The powder was found to be less effective than the cream, perhaps because it dissolves rapidly in the tissue fluids. The cream, which was applied every 24 hours, usually removed Gram positive cocci from an infected raw surface within from 4 to 6 days, but wounds tended to become soggy after it had been used for a week or more. The powder is suitable when there is only slight surface exudate from a wound, or when dry conditions are desired, but it is liable to cause a certain amount of pain. Penicillin was not found to cause any local or constitutional ill effects, and in strengths up to 20 units per square centimetre was found to facilitate skin grafting.

In affections of the eye

Von Sallmann and Meyer conducted investigations on rabbits in order to ascertain the penetration of penicillin into the eye. For iontophoretic introduction two concentrations of sodium penicillin solution were employed, 0.1 and 0.25 per cent. With a single application which lasted for 5 minutes no damage was caused except for a transient haziness of the corneal epithelium. With a 0.25 per cent solution the antibacterial activity of the aqueous was evident for almost 4 hours; the highest concentration was obtained after 45 minutes and was 32 times the amount necessary for inhibition *in vitro* of a pneumococcus culture in a dilution of 10^{-1} . The same solution applied as a corneal bath led to a maximal concentration which was more than 3 times the amount necessary for *in vitro* inhibition, and 2 hours later the aqueous still exhibited an antibacterial activity. These experiments explain the surprisingly good effects of the corneal bath in the penicillin treatment of experimental pneumococcal infections of the anterior segment of the eye. The addition of aerosol 1B in a concentration of 1 per cent to a 0.25 per cent solution of sodium penicillin, applied in the form of a corneal bath for 5 minutes, produced only slightly higher antibacterial activity than it did without the wetting agent if nupercaine (percarine) hydrochloride were used as a local anaesthetic; when general anaesthesia was employed the antibacterial activity of the aqueous was 5 times that obtained with a simple corneal bath. Penetrasol B was more irritating and less effective. Penicillin applied in salves did not produce any bacteriostatic activity of the aqueous. Similar negative results were found with repeated instillations of watery solutions. Small amounts of penicillin

entered the aqueous from the blood stream after intramuscular injection. Secondary aqueous contained several times as much penicillin as did primary aqueous.

In pulmonary disease

Post-influenzal infections.—The value of penicillin in serious pulmonary infections was tested in the winter of 1943–4 by Bennett and Parkes in a London hospital. The cases, almost all of which were complications of influenza, had resisted sulphonamide treatment and the patients were gravely ill; all recovered completely. The organisms were penicillin-sensitive. The authors point out that penicillin is not necessarily a panacea for influenza nor will it abort the primary infection. All the cases were staphylococcal infections, which are rare in influenza. The administration of penicillin reduced the amount of purulent sputum at once. In all cases there was profound asthenia for some time after the infection had cleared up. In 3 cases $1\frac{1}{2}$ million units of penicillin were given. Temperature readings and leucocyte counts seem to be the most reliable guides to suitable dosage. Penicillin was injected into the pleural cavity in cases of empyema, with good results. As even the sulphonamides have failed in local injections for empyema penicillin may be the treatment of choice in this condition. Systemic treatment may be necessary also to prevent reinfection from the surrounding tissues.

In pyogenic infections

The use of penicillin in the treatment of pyogenic infections is investigated by Florey and Williams. A group of 212 patients, the majority of whom were suffering from infections of the hand, were observed. About 50 per cent were treated with penicillin in conjunction with the generally accepted procedures and the remainder constituted a control group and were treated by routine methods. The types of lesion included paronychia, pulp infection, web-space infection, tendon sheath infection, miscellaneous abscesses, septic lacerations and other miscellaneous lesions. The patients were observed until full function had been regained or until treatment ceased. In the control group the applications used were paraffin gauze packings, eusol (solution of chlorinated lime with boric acid) solutions and saline baths. Sulphonamide preparations and gentian violet were used locally and sulphonamides were given by mouth. In the other group the calcium salt of penicillin was used for powdering the wound at operation and packs with penicillin paste were used subsequently. In the majority of cases the infecting organisms were *Streptococcus pyogenes* or *Staphylococcus aureus* or both organisms. In most of the cases treated by penicillin sepsis was more quickly controlled and the healing time was shorter. There was less pus and less pain than in the control group. A great practical advantage which resulted from the use of penicillin was the reduction in the number of dressings required. There was also a much quicker return of function and a shorter period of disability. Movements returned as soon as excess of inflammatory fluid had been absorbed. A complete return of function however was not obtained in cases of purulent tendon sheath infections. All the tendons survived in the penicillin group whereas in the other patients death of tendons occurred in 9 instances. About half the number of patients complained of burning sensations when packs with the dry calcium salt of penicillin were applied but solutions or pastes containing penicillin caused no discomfort. In 11 cases with bony involvement recalcification occurred readily. In some very chronic cases penicillin was used with good results before skin grafting was attempted. In 35 of the cases treated with penicillin, as compared with the controls, about 1,000 man days of working time were saved.

In surgical infections

Different methods of administration compared.—Observations made on the use of penicillin in the treatment of surgical infections in the United States Army are recorded by Lyons. The methods of administration included intravenous, intramuscular and intrathecal injections, and local applications of calcium and of sodium salts of penicillin. The intramuscular and constant intravenous drip methods proved in practice to be satisfactory. In cases of meningitis injections of penicillin were given into the lumbar space, the cistern and the ventricles. Various reactions which were attributed to toxic impurities were noted, including chills, headache, pain at the site of injection, faintness, muscle cramps, femoral phlebothrombosis, eosinophilia, and tingling in the testes. In a very few cases other untoward reactions occurred and did not appear to be limited to special batches of penicillin, namely urticaria—with or without pyrexia—transient azotaemia, and thrombophlebitis at the site of constant intravenous injection. The reactions were transient, and there was no evidence of persistent sensitivity. Penicillin appeared to be effective in infections with some strains of haemolytic and non-haemolytic streptococci and of staphylococci, in mixed infections due to Gram positive bacteria, in infections due to Gram negative diplococci and in the treatment of actinomycosis. The dose varied from 90,000 units given daily for streptococcal infections to as much as 600,000 units daily for staphylococcal bacteraemia. In cases of septic gunshot fracture there was often a reduced blood volume and deficiency of erythrocytes and haemoglobin. Administration of penicillin was observed to induce regeneration of these elements as a result of control of the infective process. Copious transfusions of whole blood were also given in such cases. Cases of infection by *Pyocyanus* and *Proteus* were resistant and patients with malaria did not appear to respond to administration of penicillin.

In vitro tests against various organisms

In 1929 Fleming made the chance observation that colonies of staphylococci failed to grow in the neighbourhood of a colony of contaminating mould. On examination the mould was identified as *Penicillium notatum* and in broth cultures was found to yield a soluble substance

which exerted a remarkable inhibitory effect on pyogenic organisms but not on Gram negative bacilli. Since the original discovery much work has been carried out in Great Britain and Dawson, Hobby, Meyer and Chaffee in America report on investigations which confirm and extend these results; they were able to obtain the active principles either as a salt or as a free acid. Penicillin was tested *in vitro* against a wide variety of organisms, both aerobic and anaerobic and was found to be effective against Gram positive organisms and also against the gonococcus and the meningococcus. The list of insusceptible strains include *Haemophilus influenzae*, *Bacillus coli* and the dysenteric and enteric groups. Extraordinarily high dilutions were effective. The activity was comparable with that of gramicidin and tyrocidin and was greatly superior to the sulphonamides. The action is not inhibited by blood, serum, pus or exudate. Using mice, Dawson and his collaborators found that the protective action of penicillin was much more pronounced against inoculations with highly virulent haemolytic streptococci than with *Clostridium welchii* and *Cl. septicum*. Toxic symptoms have not been encountered in man with doses far exceeding the therapeutic one but the substance is rapidly excreted from the body; at the end of 4 hours no appreciable amount can be detected after an intravenous or intramuscular injection and as a consequence frequent administration is required. The use of oily suspensions and the subcutaneous implantation of solid pellets were partly successful in animals but are not satisfactory in the human subject.

The calcium salt

Effects of intravenous and intramuscular injections.—Observations on the intravenous and intramuscular use of the calcium salt of penicillin are published by Herrell and Nichols who have not met with the complications described by Florey and who conclude, therefore, that the preparation used by them may have differed in some way from that employed by him. Preliminary experiments on the cytotoxicity to tissue cultures of this salt, of which the potency is 146 Oxford units per milligram, showed it to be somewhat less than that of the sodium salt now generally used. The minimum lethal subcutaneous dose for mice was found to be at the rate of about 500,000 Oxford units per kilogram, that is to say much in excess of that of ordinary therapeutic doses. No haemolysis of rabbit erythrocytes was observed when the animals were incubated for 2 days in contact with the calcium salt of penicillin in a plasma clot. The calcium salt was also found to be relatively stable, showing no loss of activity when kept dry for 35 days in sealed ampoules at room temperature but away from light. Twelve patients received intravenous treatment, including 5 with positive blood cultures. Four were suffering from sulphonamide-resistant gonorrhoea, 5 from staphylococcal and 3 from streptococcal infections and one from maxillofacial actinomycosis. All but 2 of the patients completely recovered including all those with septicaemia. Temporary improvement was followed by relapse in a patient with staphylococcal infection of the urinary tract complicated by stones, for which operation was subsequently required. In the patient with actinomycosis apparent cure took place but she has not been observed for a sufficient length of time to show whether the cure is permanent. The largest daily dose given was 44,000 Oxford units. No ill effects were observed. To some other patients the salt was given by intramuscular injection, again without ill effect.

Comparison of claviformin and patulin

Chain, Florey and Jennings show by comparison that the chemical properties of claviformin, a crystalline antibiotic produced by *Penicillium claviforme*, and patulin, the antibiotic recently isolated from cultures of *P. patulum*, are very similar. Indications that the two substances are identical were further strengthened by the discovery that no significant depression of the melting point of either occurred when a mixture of the two was melted. Crystallographic measurements, from which it was possible to deduce the approximate size and shape of the molecules, provided the final proof that these two substances are identical. Their biological properties were found, on investigation, to correspond. As far as its antibacterial activity is concerned claviformin, or patulin, like all ordinary antiseptics, is a general protoplasmic poison which exerts its toxic and antibacterial effect through combination with the protoplasmic constituent common to all cells and, for this reason, has not any advantage over other more readily accessible antiseptics. Results published earlier which showed that its antibacterial activity is reduced by serum and that leucocytes are killed at concentrations smaller than those required to inhibit bacterial growth, were confirmed. Any special therapeutic effect that this substance may have in the treatment of the common cold appears to depend upon whether or not it possesses any specific pharmacological properties or viricidal action apart from its antibacterial activity.

Penicillin and thyrothricin

In otolaryngology

Studies on the local use of penicillin and thyrothricin in otolaryngology have been made by Crowe, Fisher, Ward and Foley. The results of treatment in 118 patients with acute otitis media, acute and chronic mastoiditis and acute and chronic sinusitis have been better than those which the authors have ever obtained by other methods. They found that the Gram positive organisms vary in their response to these compounds; sensitivity was greatest in pneumococci and least in staphylococci; streptococci occupy an intermediate position. The sensitivity varies however in different strains; some respond to one drug and not to the other. The crude penicillin used by the authors has been tested for toxicity by administration of large and repeated doses by various routes to animals, and no ill effects have been observed.

Tyrothricin has a strong haemolytic action which prohibits its intravenous or subcutaneous use, but it is valuable for local application provided that it comes in direct contact with the organisms. Its best use is to supplement surgical operations, for example in chronic sinusitis or mastoiditis. It does not injure tissues or retard healing and by preventing post-operative wound infection greatly reduces the formation of polypi and granulation tissue and increases the likelihood of rapid and complete cure. Thus by using tyrothricin packs and irrigations after operation it is often possible to cure chronic frontal sinusitis without an extensive and deforming procedure. The authors emphasize the importance of testing the sensitivity of the infecting organism prior to instituting any form of chemotherapy.

Pethidine hydrochloride

Analgesic action in mice

Woolfe and Macdonald discuss the results of their experimental evaluation of the analgesic action of pethidine hydrochloride (dolantal). The method employed was that of applying a painful stimulus to mice. On a zinc plate which was maintained at temperatures of from 45° C. upwards, was placed a hollow glass cylinder into which the mouse was dropped, so that it was forced to walk or stand on the heated plate. The mice were tested at regular intervals after injection of the drug under test, and their reactions were noted and compared with the behaviour of mice which had not been subjected to the influence of the drug. Morphine hydrochloride was found to be an efficient analgesic against even severe pain stimuli if used in sufficiently large dosage; the duration of its effects was long and was maximal after 30 minutes. There was a great deal of irregularity in action, which was not seen to so great an extent with the use of diacetylmorphine hydrochloride. Very considerable variation in response was also seen with codeine hydrochloride and effective dosage approached the lethal dose. Dolantal produced prolonged analgesia against mild pain stimuli but it was ineffective against severe pain stimuli of the type used; analgesia reached its maximum intensity in about 25 minutes. Phenobarbitone had no analgesic effect in doses lower than the anaesthetic range. Amidopyrine and antipyrin were effective only in very large doses and aspirin had no analgesic action. It was concluded that dolantal had from one-fifth to one-sixth of the analgesic activity of morphine hydrochloride against mild stimuli but was ineffective against severe pain.

Promanide

Therapeutics and toxicology in tuberculosis

Steenken, Heise and Wolinsky report further experiments in the treatment of experimental tuberculosis in guinea-pigs with promin (promanide). Sixty tuberculin-negative guinea-pigs each weighing 300 grammes were used. Of these, 20 were vaccinated with living H37 R₁ tubercle bacilli before the experiment so that they were rendered tuberculin-positive and these, together with 20 unvaccinated animals, were given 150 milligrams of promin orally every day while the experiment was in progress. Two days after the experiment began all the 60 animals were injected subcutaneously with 0.5 cubic centimetre of a suspension of H37 R₁ micro-organisms which had been grown on Proskauer and Beck's synthetic medium for 14 days. Each dose contained approximately 10,000 organisms. The results afforded striking evidence of the retarding influence of promin on the development and progress of the tuberculosis; the effects were more pronounced in the case of the animals which had previously been inoculated with the non-virulent strain. Of the control group 12 animals died of tuberculosis before the end of the experiment and of the non-vaccinated group treated with promin one died of tuberculosis and 3 of non-tuberculous conditions, whereas all animals in the vaccinated and treated group survived until the experiment was terminated by killing them on the 224th day. The necropsies showed that 7 of the last group had not any macroscopical disease and in the remaining 13 the involvement was slight. All the treated animals gained weight until the end. No toxic manifestations were noted. In order to study the toxic effects more fully 5 normal guinea-pigs were fed with 150 milligrams of promin twice daily for 35 days. All showed a moderately severe haemolytic anaemia. A dose of 600 milligrams twice daily proved fatal to 3 guinea-pigs within 5 days. In the treated animals the average blood concentration of promin was between 4 and 6 milligrams per 100 cubic centimetres of blood. In other animals experiment showed that a single dose of 300 milligrams of promin caused a maximum blood concentration of 22.5 milligrams per 100 cubic centimetres in 12 hours, after which the concentration fell rapidly and only a trace remained at the end of 24 hours.

Promizole

Toxic reactions

Higgins and Larson studied some of the toxic reactions of 4 : 2'-diaminophenyl-5'-thiazole-sulphone (promizole) as the course of experimental tuberculosis in guinea-pigs had been favourably influenced by its administration. Other workers had shown that thyroid hyperplasia is prevented by administration of an adequate amount of iodine when such goitrogens as cabbage, soya bean flour, methyl cyanide or potassium thiocyanate are given. Although thyroid hormone or desiccated thyroid can prevent hyperplasia of the thyroid gland which is induced by such new goitrogens as sulphaguanidine, phenylthiocarbamide and many compounds containing thiourea, iodine apparently cannot. The writers gave daily doses of 25 milligrams of promizole to young rats which became alopecic and showed noticeable thyroid hyperplasia; the colloid became stringy and the pituitary glands were like those of thyroid-

ectomized animals. Large portions of the bodies were found to be denuded of hair after the animals had been licking themselves evidently in an attempt to derive from the hair an essential metabolite which was denied them by promizole. The preliminary report also tends to show that promizole retards rate of growth, does little damage to blood corpuscles and needs less than 2 weeks to cause manifest destruction of the colloid in the acini with increased height of the acinar cells. There was distinct proliferative reaction in the experimental animals after promizole had been administered by stomach tube for 8 weeks. The rats had been on a purified diet with adequate amounts of cod-liver oil and vitamin B.

Propamidine

Uses in jelly and in saline form

Butler reports on 10 cases treated with propamidine. Two preparations were used. (1) An 0.1 per cent jelly which was applied to wounds after they had been cleaned with saline, by means of a spatula. The wound was then covered with gauze impregnated with liquid paraffin to prevent the jelly from drying. The application was renewed every second or third day for a total period of 10–14 days. The results were encouraging, but certain limitations are pointed out. (a) The jelly base is irritating to tissues and must not be used in sutured wounds; the skin should be protected by soft paraffin. (b) If propamidine is used for more than 10 days the production of granulation tissue is apt to be excessive. (c) Propamidine jelly is essentially a local bacteriostatic and must be applied to the entire surface of a wound; the drug does not penetrate soft tissues or bone. (d) Wounds rarely become sterile under treatment but healing seems to be accelerated. (2) A 1 per cent solution in saline, of which an amount not exceeding the equivalent of 2 milligrams per kilogram of body weight was injected into infected serous or synovial cavities. It appeared to be of value in overcoming joint infections but to be ineffective in empyema.

Sodium amytal

Use in psychosis

The reaction of a psychotic patient to the intravenous injection of sodium amytal is of diagnostic, therapeutic, prognostic and investigative importance. Drowsiness and shortness of reaction frequently mask the desired effect. In an attempt to lessen drowsiness and prolong the reaction various stimulants of the central nervous system have been employed. Gottlieb and Coburn have studied the psychologic effects in schizophrenic and depressive patients of the intravenous administration of sodium amytal and of the stimulant, amphetamine (benzedrine) sulphate, alone and in various combinations. Twenty consecutive patients who were suitable for testing, 10 of whom had schizophrenia and the other 10 depressions, were subjected to the following routine procedure. On 5 successive days the patient was given one of a series of intravenous injections early in the morning, the type and duration of the response and the degree of narcosis being noted. The doses of the drugs were always the same: 250 milligrams of sodium amytal and 10 milligrams of amphetamine sulphate. In the first injection sodium amytal alone was given; in the second amphetamine sulphate; in the third sodium amytal followed immediately by amphetamine sulphate; in the fourth amphetamine sulphate followed by sodium amytal; in the fifth a mixture of the two drugs. The reactions as described in the paper were evaluated as good, moderately good and poor. In the group of depressed patients it was found that the psychological characteristics of the reactions were not significantly changed by the addition of amphetamine sulphate to the sodium amytal but the duration of the response was increased and the narcotic effects were less prominent. In contrast the schizophrenic patients showed on the average the same length of response and a poorer psychologic reaction; in some patients the responses became shorter. This may have been due to the observed phenomenon that subsequent responses to sodium amytal in schizophrenics often become poorer and is consistent with the tolerance which is known to develop towards the barbiturates. Such tolerance was not observed in the patients with depression.

Sulphonamide compounds

Absorption rate

Tests with powder and oily suspensions.—The efficacy of sulphonamides when used against streptococcal and gas gangrene infections is proportional to their powers of permeation and especially to the interval of time after injury after which they can be applied. Magner and O'Sullivan therefore advocate the inclusion of sulphonamides in first field dressings. Sulphathiazole powder and 10 per cent of sulphathiazole in normal saline solution and in 6 varied suspensions, constituted the 8 preparations used for an investigation of the absorption rate and of the effect thereon of fine pulverization and of adding wetting agents to oily suspensions. In 3 suspensions hydrocarbon oil—compounded of 44 grammes of paraffin oil, 2 grammes of triethanolamine and 6 grammes of oleic acid—was the vehicle employed, either alone, or with 0.15 per cent aerosol as wetting agent, or emulsified in water. These three preparations, each of which contained 200 milligrams of finely pulverized sulphathiazole in oil, were designated colloidal sulphathiazole; they were inserted into the incised thighs of guinea-pigs and the sulphathiazole blood concentration was estimated at intervals. In order of rapidity of absorption emulsions came first, then oils, then saline solution and lastly powder. Further, pulverization and the addition of the wetting agent were found to accelerate the rate of absorption. Next, the thighs of 3 groups of guinea-pigs were incised and infected with *Clostridium*

welchii. The wounds of control group (1) and of group (3) were immediately sutured; those of group (2) were sutured after the powder had been packed in or an intramuscular injection of the fluids had been given. The wounds of group (3) were reopened and medicated after a delay of 2½ or 5 hours. From the different results obtained the facts emerged (1) that immediate treatment achieved success approaching 60 per cent, (2) that success after a delay of 2½ hours exceeded 50 per cent—a success much enhanced when the quantity of sulphathiazole given was increased from 50 to 100 milligrams—and (3) that the mortality of controls and of animals treated after 5 hours was practically 100 per cent. Unexpectedly, rapid absorption did not appear to diminish mortality. Although the slowly absorbed powder is equally bacteriostatic the more penetrating oil-aerosol suspension may yet prove to be superior in treatment of deep lacerated wounds.

Methods of administration and some newer compounds

Fitch publishes further observations on the sulphonamide compounds and on the relative values of different methods of administration. The problem of sulphonamide sensitivity is discussed; 10 per cent of patients treated with sulphonamides may become intolerant to them and 33 per cent may show allergic reactions to sulphathiazole. The danger of sensitivity to sulphonamides is apparently increased when administration is continued for more than 5 or 7 days and sensitivity may last as long as 15 months. Satisfactory results continue to be reported from the treatment of burns by sulphanilamide in the form of an ointment. Sulphanil mandelate is a new compound devised for treatment of uncomplicated bacillurias. Sulphathiazole has been prepared in the form of microcrystals which are readily soluble and consequently have a rapid action after local application. In impetigo sulphathiazole has been found to give a more satisfactory result than do other sulphonamide compounds. The use of succinylsulphathiazole has been investigated in infections of the alimentary tract and has been found to give as good results as does sulphaguanidine. Sulphathiazoline is slightly less toxic in action than sulphathiazole and has been found useful in anterior gonorrhoeal urethritis in men. Sulphapyridine is still commonly used in the treatment of the pneumonias and it appears that a 40 per cent solution of sodium sulphapyridine may prove useful as a haemostatic in secondary haemorrhage occurring after tonsillectomy. Sulphacetamide is used in infections of mucous membranes. Sulphadiazine probably causes toxic effects less commonly than do other sulphonamides and under daily observation may be given to patients who already have acute toxic reactions due to sulphonamide therapy. The compound also gives favourable results in the local treatment of burns and in cranial wounds. In lobar pneumonia sulphamethazine (sulphadimethylpyrimidine) compares favourably with sulphapyridine and as it is readily absorbed and slowly excreted administration is required less often. Sulphapyrazine, phthalyl-sulphathiazole, promanide and diphenylsulphone-4 : 4'-bisazosalicylic acid are among the other newer compounds which have been prepared in the past 2 years.

Application in cases of bacterial infection

Osgood discusses the indications for the use of chemotherapy in bacterial infections which are encountered in general practice. The sulphonamides alone are dealt with, penicillin being excluded. The majority of virus diseases are unaffected by the drugs, which should not be employed in the common cold, simple pharyngitis, influenza and the virus pneumonias unless secondary bacterial complications supervene. Tuberculosis, fungus infections and rickettsial diseases are not influenced by sulphonamides. It must be remembered that the compounds are toxic and should be used only if the systemic infection is of a serious nature. Sulphadiazine is the drug of choice for use in meningitis, succinylsulphathiazole in bacillary dysentery and sulphathiazole in infections by the other types of organisms which have proved susceptible to the sulphonamide group. Osgood considers that there is no reason for the use of sulphanilamide in infections since it is much less effective than the other sulphonamides. The optimal concentrations in the blood per 100 cubic centimetres are from 4 to 8 milligrams of sulphathiazole and from 16 to 32 milligrams of sulphadiazine. The author recommends the use of neoarsphenamine in pneumonia, bacteraemia, endocarditis or meningitis due to staphylococci, β -haemolytic streptococci or *Streptococcus viridans*; it is also of value in meningococcal, gonococcal and influenzal (*Haemophilus influenzae*) conditions which are not responsive to sulphonamide therapy. The optimum concentration of neoarsphenamine corresponds to from 75 to 200 gammas of arsenic per 100 cubic centimetres of blood. In both arsenical and sulphonamide treatment a rapid attainment of the optimal blood concentration is indicated. In between 2 and 5 per cent of any treated series of patients complications may be expected to develop with a certain number of deaths directly attributable to the drugs themselves. Mild toxic reactions are seen in an additional 5 to 15 per cent. For local use the compound of choice is sulphathiazole. Emphasis is laid on the importance of not disregarding other forms of treatment which have been well established in the particular disorder. Daily leucocyte counts, haemoglobin estimations and records of urinary output may forestall death due to toxicity of the drugs; vitamin B is also helpful and barbiturates may decrease the tendency to nausea and vomiting.

In children's respiratory diseases.—The use of sulphonamides in the treatment of respiratory infections in children is discussed by Janeway. These diseases may be caused by either a virus or a bacterium. The sulphonamides are fairly effective against almost all the bacteria which cause respiratory infections, with the possible exception of the staphylococcus, but virus infections are not influenced by them. Sulphonamides therefore should be reserved for cases of

bacterial infection; they need not be given in every instance, but only when the child is suffering from a spreading infection, for this is the type which is dangerous. Fever and leucocytosis are not always present in children, even in bacterial infections. The child's general condition is the best guide. If he is prostrated and fretful, vomits and refuses his food, a greater risk is run by withholding than by giving sulphonamides. Adequate doses must be given and in 2 or 3 days it will be possible to judge the effect. Sulphadiazine is the best because it is the least toxic of the sulphonamides, but supplies are short and it may be necessary to substitute sulphathiazole. The latter however is much more rapidly excreted, and thus it is difficult to maintain an adequate concentration in the blood without producing renal complications. Children with a severe infection often become dehydrated and it is particularly important to administer enough fluid to maintain a proper flow of urine. The dosage is usually 1 grain per pound of body weight for the first 24 hours. In severe cases $\frac{1}{2}$ or $\frac{3}{4}$ of this amount is given as an initial dose. In pneumonia the initial dose is $\frac{3}{4}$ grain per pound and then 1 grain per pound per day. Subcutaneous administration may be necessary if vomiting is obstinate. Careful watch must be kept for signs of poisoning.

In acute and in chronic liver disease

Sulphadiazine and its reactions.—Thirty-seven patients who presented evidence of acute or chronic liver disease and who, for various reasons, required sulphonamide therapy, were studied by Peterson, Deutsch and Finland in order to ascertain the possibility of further liver damage attributable to the treatment. In 13 cases of acute hepatitis the patients showed a striking response and most of them made complete clinical recovery. The remaining subjects were affected with chronic liver disease and in them the results were not so striking, but sulphathiazole and sulphadiazine did not produce any further liver dysfunction as measured by hepatic efficiency tests; in some cases it decreased during the treatment. Among the 14 cases of portal cirrhosis the authors found a great incidence of toxic reactions; liver disease secondary to cardiac failure was not adversely affected. The general conclusion reached was that the presence of liver damage is not considered to be a contra-indication to the administration of sulphonamides to patients in whom those bacterial infections against which sulphonamides are effective, are present. Sulphadiazine is the drug of choice. Caution must be exercised in the administration of sulphonamide compounds to patients with portal (Laennec's) cirrhosis. It must be remembered that many cases of liver damage secondary to sulphonamide administration have been reported, for example in patients with drug sensitiveness or idiosyncrasy, and when considerable retention of the drug has occurred because of renal insufficiency or because excessive and toxic doses had been employed.

Effect on the skin

In order to justify the risk of skin sensitization inherent in the local application of the sulphonamides, their superiority to trusted remedies must be established. Barber, sceptical about the superiority, cites the conflicting evidence of authorities regarding sulphonamide sensitization in general and the particular preparation likely to prove toxic. Sulphadiazine cream is a routine application for impetigo in the United States Army, but a British hospital in the Middle East within 6 months admitted 55 cases of sulphanilamide dermatitis. The statements of those who have treated hundreds of pyodermites with sulphathiazole paste without casualty must be respected, yet an Army Medical Department Bulletin gives the warning that sensitization is especially liable to follow administration of sulphathiazole. Sensitization affects the Malpighian cells; therefore sulphonamides can be safely applied to wounds and burns below this layer. Both in local and in oral use allergic hypersensitiveness which yields to continued administration must be distinguished by Werner's test of sulphonamide excretion from toxæmia of retention which necessitates immediate cessation. These risks are diminished, not abolished, by limiting local applications to 5 days and oral administration to 7 days. Orally the sulphonamides are rationally employed in acute infections, in chronic conditions reputedly infective and in eruptions probably bacteriaemic. Erysipelas is undoubtedly the most favourable field. In acute or chronic streptococcal infections sulphonamides may be of great value. The sulphonamide treatment of streptococcal lupus erythematosus presents peculiar dangers which require confinement of the patient to bed under remitting surveillance. In staphylococcal infections, acute and chronic, favourable but transitory results are reported from the use of sulphathiazole; similar reports are given of sulphapyridine in virus infections. The erythemas of bacteriaemia may respond to sulphonamides if closed foci are eliminated but minimal doses must be given at first to determine tolerance. For chronic as for acute cases a short course is to be preferred, exemplified, in an acute case of impetigo contagiosa, by sulphathiazole 2 grammes at 8 a.m., 4 p.m. and bedtime on the first day and 1.5 grammes at the same hours on 3 succeeding days. It is important to ascertain that previous sulphonamide treatment has not sensitized the patient, or else violent reaction may ensue.

Heathcote expounds the pharmacology of the sulphonamides and Pillsbury their topical application in dermatology. An essential metabolite to most organisms is *p*-aminobenzoic acid, which sulphonamides displace. Their battleground is the enzyme of growth of the organism; if this is occupied by the victorious sulphonamide, the organism cannot utilize it and is inhibited. If *p*-aminobenzoic acid is simultaneously administered the sulphonamide is outflanked and its bacteriostatic power nullified. *Streptococcus faecalis* is insusceptible, *Streptococcus haemolyticus* susceptible; this illustrates natural drug resistance. Acquired resistance is shown by means of growing organisms in progressive strengths of sulphonamide

until a culture flourishes in a concentration which would be fatal to the parent strain. Hence the necessity to initiate treatment with large doses in order to obtain quickly a high sulphonamide blood concentration. Drug-fastness once established is permanent, and fastness to one member of the sulphonamide series involves fastness to all. Pyrexia encourages metabolism. If, as averred, the action of sulphonamides is on the metabolism of organisms, their potency against virulent and pyrogenic organisms is explained, as is the value of hyperthermia in treating the febrile disease, gonorrhoea. The laboratory cannot yet support the clinician's preference for applying different sulphonamides to different organisms. Skin conditions treated by sulphonamide application comprise (1) primary and (2) secondary acute superficial infections, (3) chronic eczematous conditions possibly involving infection, (4) chronic ulcers and (5) cellulitis. Chronic pilosebaceous infections yield disappointing results. (1) Impetiginous infections require daily washing and the removal of crusts, by compress if necessary. Sulphathiazole ointment should be rubbed in 3 times daily; the application should be limited to 5 days in order to avert sensitization. (2) Lesser success attends sulphonamide treatment of secondary superficial infections—which must be swiftly eradicated before they invade the underlying lesions—such as fungous infections and seborrhoeic dermatitis. (3) Chronic eczematous conditions cover a wide field peculiarly liable to sensitization to sulphonamides; local application is therefore contra-indicated. (4) Ulcers promise moderate success, with the exception of those due to syphilis, diabetes or vascular conditions or which contain micro-aerophilic streptococci insusceptible to sulphonamides. Ointments of the emulsion type, either oil-in-water or water-in-oil, are most generally acceptable. The menace of sensitization, although to some extent controlled by means of a limit to the duration of application, leaves the sulphonamides as incompletely justified adjuvants in dermatology until compounds which carry less risk of sensitization than those now available are to be had.

Experiments on the rabbit's eye

The results of a study made by Bellows and Gluckman suggest that sulphonamide compounds have a local toxic effect on actively growing epithelium, more than doubling the time required for regeneration and increasing the amount of scarring. Their experiments, carried out on young adult rabbits, consisted in removal of the corneal epithelium from both eyes by rubbing them with gauze after anaesthetization with cocaine. Fluorescein was used to make certain that the epithelium had been completely removed. One of the sulphonamides was then applied to one eye as powder, or as a 5 per cent ointment or a 20 per cent suspension. The drug to be tested (sulphanilamide, sulphathiazole, sulphapyridine or sulphadiazine) was applied 3 times daily, the other eye serving as control. Fluorescein was used after the course of epithelial regeneration. The reactions to all these compounds were similar in kind and degree. Regeneration of the corneal epithelium in the untreated eyes was rapid, healing being complete in an average of 5.1 days. In the treated eyes the process of healing occupied an average of 13.3 days, and in some cases healing appeared to be at a complete standstill until the drug was stopped. Scarring occurred in all the treated corneas.

Sulphamerazine

In bacterial infections.—Two hundred and ten adults and 68 children under 12 years of age were treated for bacterial infections with sulphamerazine (2-sulphanilamido-4-methylpyrimidine) by Anderson, Oliver and Keefer; quicker absorption from the gut and slower excretion by the kidneys give this compound blood-concentration superiority over sulphadiazine; doses from one-half to one-third smaller as well as longer intervals between doses are required. Adults, and children over 60 pounds in weight, were given 2 grammes initially and 1 gramme every 8 hours thereafter. Children under 60 pounds were given 0.5 gramme initially and a daily maintenance dose of 0.5 gramme for each 10 pounds of body weight given in 3 equally divided doses at 8-hourly intervals. Oral administration was exclusively used in most cases but in a few severely ill patients the 5 per cent solution of the sodium salt in distilled water was given intravenously during the early part of the illness. Sulphamerazine exhibited a therapeutic efficiency similar to that of sulphadiazine in the treatment of pneumococcal pneumonia, meningococcal meningitis and erysipelas. Beneficial results were obtained in other infections but are not specifically claimed for various reasons such as too small a group for statistical analysis and the employment of multiple therapeutic measures. Staphylococcal infections remained uninfluenced by the compound and no significant improvement occurred in subacute bacterial endocarditis caused by *Streptococcus viridans*. Toxic reactions which were not sufficiently severe to jeopardize health or to cause serious discomfort occurred in 70 cases and were of the same character and happened about as often as did those which were caused by sulphadiazine. There was however a greater tendency with sulphamerazine for crystalluria, leucopenia, drug rashes and drug fevers to develop.

Assessment of toxicity.—Sulphadiazine, the least toxic of the sulphonamide compounds, provides the gauge against which the toxicity of the more recently synthesized sulphamerazine is assessed by Dowling, Dumoff-Stanley, Lepper and Sweet. The curative value of the compounds appears to be equal. As regards vomiting and mental confusion, neither preparation took precedence. Sulphadiazine produced, in 900 patients, 4 instances of haemolytic anaemia or of leucocytosis. Sulphamerazine (428 patients) did not produce any. Sulphadiazine produced fever, dermatitis or conjunctivitis in 2.9 per cent of cases and sulphamerazine in 3.7 per cent. These data are not of statistical significance. Renal pain, haematuria, anuria or oliguria were accepted as evidence of renal calculus formation. A percentage of 3.5 instances after sulpha-

merazine administration, contrasting with 1·3 after sulphadiazine, is considered to be significant. An oral dose, larger or smaller, of sulphamerazine produces a drug level in the blood of greater average than does an equal dose of sulphadiazine; this suggests that a relatively smaller dose of sulphamerazine would be efficient. It is probable, however, that twice as much sulphamerazine as sulphadiazine is bound to serum proteins and rendered therapeutically inert. A higher blood level of sulphamerazine is therefore necessary in order to attain a therapeutic effect equivalent to that of sulphadiazine. This higher level involves the increased risk of renal calculus. Sulphadiazine retains its pre-eminence unless in certain cases it is found to be unsuitable. Then only is sulphamerazine a desirable substitute.

Comparison with sulphadiazine in clinical series.—A series of 116 patients treated with sulphamerazine and its sodium salt is recorded by Hall and Spink. Sulphamerazine is the monomethyl homologue of sulphadiazine. It is claimed that higher blood levels can be attained by the use of sulphamerazine than by giving equivalent doses of sulphadiazine. It is more soluble in urine and is excreted more slowly, therefore the risk of crystalluria should be less. In the present series the following results were obtained. (1) Forty-seven patients with pneumonia were treated for from 5 to 7 days with an initial dose for adults and older children of from 3 to 4 grammes followed by 1 gramme every 6 hours, subsequently reduced to 0·5 to 1 gramme every 8 hours. In small children and infants the initial dose was 0·04 gramme per pound body weight (not over 4 grammes) followed by 0·05 gramme per pound daily in divided doses. The results appeared to equal those obtainable with sulphadiazine. (2) In 11 patients with staphylococcal sepsis, including 2 with positive blood cultures, sulphamerazine appeared to be less effective than sulphadiazine would have been. (3) Thirty-three patients with streptococcal sepsis responded as well to sulphamerazine as a comparable control group did to sulphadiazine. (4) Five patients with meningitis due to the meningococcus or the influenza bacillus recovered. (5) In the remainder of the patients, with miscellaneous infections, the results appeared to equal those given by sulphadiazine in similar cases. The authors confirm the claim that large blood concentrations of sulphamerazine can be achieved by giving comparatively small doses. Toxic manifestations occurred in 13 cases, including one instance of anuria and one of oliguria. One of these patients had been taking ammonium chloride and it is thought that the high acidity of the urine (pH 4·6) was an important factor in causing precipitation of crystals in the urinary tract.

Comparison with sulphathiazole and sulphadiazine.—One of the difficulties in the administration of sulphathiazole and sulphadiazine is the tendency of these drugs to produce crystalluria and haematuria, especially in warm climates where the urinary output is meagre. Hageman, Harford, Sobin and Ahrens publish a study of 103 cases treated at the Barnes Hospital and the St. Louis City Isolation Hospital with sulphamerazine (2-sulphanilamido-4-methylpyrimidine) which is 20 per cent more soluble in water and in urine than is sulphadiazine, is more rapidly and completely absorbed from the gastro-intestinal tract and is more slowly excreted. For these reasons it was hoped that satisfactory blood concentrations might be attained with smaller and less frequent doses of the new compound, and urinary complications avoided. The routine dosage was an initial dose of 4 grammes followed by maintenance doses of 1 gramme every 8 hours. In severely ill patients this dosage was doubled. Blood concentrations were measured at least every 24 hours just before an 8-hour maintenance dose was administered, and if the blood concentration did not attain the desired levels supplementary doses were given occasionally. A urinary output of a litre or more in the 24 hours was aimed at. Urine analyses were performed daily, the microscopic examination being made immediately after the urine was voided. Blood counts and haemoglobin determinations were made every 3 days during treatment. Both rapid absorption and the maintenance of large blood concentrations were well shown. The therapeutic results in meningococcal, pneumococcal and streptococcal infections were satisfactory. Drug fever was noted in 6 instances and a morbilliform rash was observed twice. Neuropathological changes, agranulocytosis, anaemia, nausea and vomiting were not observed. The compound readily diffuses into pleural fluid in concentrations approximately that of the blood and into spinal fluid in concentrations approximately 50 per cent of that in the blood. Heavier dosage is therefore desirable in meningococcal cases. Haematuria was observed in 9 instances (8·7 per cent). Three of these patients showed crystalluria and crystalluria without haematuria was noted in 7 patients (6·8 per cent). In one fatal case of a patient who showed no crystalluria or haematuria during life, concretions of sulphonamide crystals were found in both ureters at necropsy but this patient had received sulphapyridine after sulphamerazine treatment had been stopped. Certain conclusions could not therefore be arrived at over the greater or less frequency of urinary complications after treatment with sulphamerazine than after treatment with sulphadiazine.

Sulphanilamide

Sulphanilamide lozenges in tonsillitis and influenza.—Garson has tried local oral chemotherapy by means of sulphanilamide lozenges for 86 patients with acute tonsillitis and 69 with influenza. The patient was given 8 lozenges, each containing 0·065 gramme of sulphanilamide, one to be sucked each hour between 8 and 11 a.m., one at 4 p.m., two after the evening meal and one at bedtime; the total daily dose was thus 0·52 gramme of sulphanilamide. It was found that this method of local treatment reduced the average stay in hospital, as compared with a control series, by 2·5 days for tonsillitis patients and by 3·3 days for influenza patients. Relief of pain was a striking feature of the treatment, often noted within 2 hours. Prophylactic-

ally, 4 lozenges a day appeared to diminish the incidence of these ailments: for instance, of 100 recruits who received lozenges tonsillitis developed in one, whereas among 140 controls 14 cases occurred.

Sulphapyrazine

Results in pneumonia.—The results of treatment of 105 cases of pneumonia with sulphapyrazine, an isomer of sulphathiazole, are presented by Rueggsegger, Brookens, Hamburger and Grupen. At first the oral route was used exclusively, the initial dose of 2 or 3 grammes being followed by doses of 1 gramme every 4 hours. Later, the initial dose of 4 grammes intravenously was followed by oral doses of 1 gramme every 6 hours. In a control series, 133 patients were treated with sulphathiazole. Bacteraemia was present in 24 of the sulphapyrazine treated group and 26 of the controls. The total mortality was 4 per cent in the sulphapyrazine-treated and 7 per cent in the control group. Among the non-bacteraemic patients the mortality was 0 and 4 per cent respectively, among the bacteraemic patients 17 and 19 per cent. In none of the sulphapyrazine-treated patients did any purulent complication develop under treatment. One patient was admitted with an empyema which had to be drained, another with two pyarthroses which subsided. Oliguria and haematuria occurred 5 times, but after the dosage was reduced the only cases of renal damage were an occasional microscopic haematuria. One case of morbilliform rash and one of vomiting occurred.

Sulphapyridine

Radical treatment of sulphapyridine anuria.—Campbell has experience of 6 patients with sulphapyridine anuria which did not respond to conservative treatment. Five of the cases cleared on ureteric catheterization and one patient was relieved by pyelostomy after it had been found impossible to pass a catheter. In early cases in which the urinary output has stopped within the previous few hours, fluids should be given intravenously. Except in such very recent cases, cystoscopy should be carried out at once, the ureters should be catheterized and the pelvis washed out. Furthermore, if renal colic is severe and oliguria and haematuria occur, and if the administration of intravenous fluids with diuretics fails to increase the output, catheterization should be carried out. For the purpose of making a check of renal function, Campbell recommends that intravenous pyelography be done one week after the anuria has been relieved. He finds that the nature of the crystalline impaction and the consequent difficulties in catheterization vary directly with the time that has elapsed since the gross haematuria began. Patients who cannot be relieved by cystoscopic measures should be treated by pyelostomy or nephrostomy. Unilateral operation is adequate if the pelvic contents are fluid for it is likely that the ureters can be catheterized a few days after the relief of the anuria. Bilateral pyelostomy or nephrostomy and decapsulation should be done only in the very delayed type of case in which at operation no secretion occurs after the emptying of a pelvis.

Sulphathiazole

Use in general surgery.—The value of sulphathiazole in general surgery is discussed by Serino, who points out that its use does not excuse any neglect of well-tried surgical principles. In 207 cases of infection sulphathiazole was employed as an aid to surgery, because as compared with other sulphonamides its range of bacteriostatic usefulness is wider, absorption and excretion are more rapid and toxicity is less. No rigid schedule of total dosage was adopted. For severe infections the initial dose was 3 grammes repeated in 4 hours and afterwards doses of 1 gramme were given 4-hourly day and night as long as infection appeared to be spreading. In moderately severe cases the dosage was 2 doses of 2 grammes at 4 hours' interval and subsequently 1 gramme 4-hourly. Treatment was continued for at least 48 hours after clinical signs subsided. The drug was given by mouth except when it was not tolerated, and then it was given by intravenous drip. The blood count and haemoglobin determination were carried out on admission and every 2 or 3 days afterwards, and the blood concentration of sulphathiazole was estimated daily in most cases; it varied from 5 to 15 milligrams per 100 cubic centimetres and served as a guide to dosage. In some cases sulphathiazole was used as a local application before wounds were sutured. It was found that the best results were obtained when small amounts locally were supplemented by oral administration; in large quantities sulphathiazole tends to cake and produce pressure necrosis of skin edges. Applied locally to chronic ulcers and burns, sulphathiazole gave satisfactory results in 24 patients. In peritonitis of appendicular origin the death rate was lower in patients treated with sulphathiazole than in a control group treated by operation alone. Toxic symptoms occurred in 27 patients, but in no case were they of a serious character.

The hypersensitive person.—That local sulphathiazole therapy can induce cutaneous sensitivity is confirmed by 4 cases reported by Shaffer, Lentz and McGuire and 26 others collected by them from the literature. Their cases were as follows. (1) A housewife of 28 years of age had a chronic staphylococcal dermatitis of one hand, for which X-ray therapy, sulphathiazole ointment and injections of staphylococcus ambotoxoid, 5 per cent, were prescribed. By the end of the third week of treatment the process had become very acute and the other hand was involved. Treatment was stopped and the dermatitis reverted to its previous chronic state. Attempts to desensitize the patient to staphylococcus ambotoxoid resulted in acute exacerbations and this treatment was abandoned. One week later sulphathiazole was begun in oral doses of 1 gramme every 6 hours. Immediately after the first dose had been given the dermatitis began to flare up and after 2 doses a generalized papular and urticarial rash

appeared. This subsided in 3 days, but the local process on the hands took over 6 weeks to do so. The patient then by mistake applied sulphathiazole ointment again and within 24 hours a generalized and much more severe eruption developed, which subsided only after 4 months of palliative treatment. (2) A youth aged 21 years with a relapsing purulent staphylococcal eruption of the scalp and ears was treated orally with sulphanilamide and then with sulphathiazole. After 8 days the eruption had gone. One month later he had a relapse after an initial injection of staphylococcus ambotoxoid, and after unsuccessful attempts at desensitization, treatment with 1 per cent sulphathiazole ointment was begun. The eruption became worse and a generalized vesiculo-pustular rash appeared. On 3 subsequent occasions he was treated for relapses with sulphathiazole ointment or tablets and on each occasion an acute exacerbation took place. (3) A man aged 27 years with contact dermatitis of both hands was treated at first with sulphathiazole ointment, 6 per cent, and later, as he failed to improve, with sulphathiazole orally. After 3 days a generalized eruption appeared, which subsided when sulphathiazole was stopped. (4) A boy aged 16 years with acne vulgaris was treated with a lotion containing 3 per cent of sulphathiazole. After 6 weeks of treatment dermatitis developed; when the patient stopped using the lotion it subsided, but reappeared each time the lotion was applied. The same lotion with sulphathiazole omitted did not produce any ill effects. In 3 patients examined, cutaneous sensitivity to sulphathiazole was demonstrated by passive transfer tests.

Sulphonamide powder in operation wounds

Key advocates routine implantation of sulphonamide powder in clean operation wounds in order to prevent infection and cites a series of 600 clean orthopaedic operations in which the total post-operative complications which occurred comprised 3 deaths, 7 haematomas, one separation of wound margins, 2 stitch abscesses and 2 infections. The only toxic symptom was fever. The fatalities were not related to the sulphonamide treatment or to infection. Haematomas developed in the wounds of 5 patients who had had local anaesthetics containing adrenaline; with such technique the ligature of small vessels may be omitted. In the case of separated margins the uninfected wound healed after it had been sprinkled with sulphathiazole. Of stitch abscesses the first developed in a man over 80 years old, who was irrational and intolerant of his dressings. He died 63 days after operation, the wound being healed. In the second case, that of a woman, stitch abscesses developed 6 days after operation. She had 5 times previously had cutaneous abscesses around the knee concerned. The 2 infections were mild, late and avoidable; the first arose from parental neglect of a dressing after the boy's discharge from hospital and the second from late evacuation of a haematoma. These results compare favourably with the general incidence, approximately 5 per cent, of infection in clean operations. Sulphanilamide 2 parts and sulphathiazole 1 part form the mixture used but either compound serves alone. The drugs, if not obtained in sterile packets, require sterilization in the autoclave. Usually less than 5 grammes are distributed from a sterilized dredger. In a clean wound 10 grammes was never exceeded. Crystals cover less surface per gramme. A gramme of the substance may be dropped and smeared in a large joint before the synovial surface is closed.

Tannic acid

Toxicity

Experimental evidence.—In experiments on the toxicity of tannic acid Cameron, Milton and Allen employed a 5 per cent solution of tannic acid (B.P.), which contained about 20 per cent of gallic acid, in distilled water. This solution is almost isotonic. Goats, rabbits, guinea-pigs and rats were used and administration was made intravenously and subcutaneously and by the spraying of burned surfaces. In cases rapidly fatal from intravenous injection death was due to respiratory failure. Necropsies were performed on all animals which died and on surviving animals which were killed at intervals during 4 weeks, so that the pathological course could be observed. All organs and tissues were examined histologically. Centrilobular hepatic necrosis and exaggerated capillary permeability were the outstanding features. Renal changes although constant were slight and transient. There was evidence of bone marrow stimulation. There was not any ecchymotic effect in pregnant females. Blood changes were shown by the presence of leucocytosis, by increased haemoglobin percentage, in the erythrocyte count and in the haematocrit value. There was a fall in total blood and plasma volume but not in corpuscular volume. The ferric chloride reaction was used in order to estimate the amount of tannic acid in the blood and a method of differentiating between tannic and gallic acid, based on the oxidation of gallic acid in alkaline solution to a coloured quinonoid complex, proved that gallic acid was not the cause of the pathological changes. Erb, Morgan and Farmer who have recorded the findings at necropsy in 41 cases of burns in human beings which were treated with tannic acid, reported liver necrosis in 25 and renal changes in 18 cases. Among 20 untanned fatalities there was one case of renal but not any of hepatic damage. The authors note that evidence which demands the critical revision of tannic acid treatment is accumulating.

Thiourea

Experimental work on rabbits

Baumann, Metzger and Marine performed experiments on rabbits to determine the mode of action of thiourea (sulphocarbamide, $\text{CS}(\text{NH}_2)_2$) on the thyroid gland. Previous investigators have found that neither iodides, various members of the vitamin B group nor vitamin

C could prevent the development of goitre, whereas hypophysectomy or the administration of thyroid or thyroxine did so. Intraperitoneal thiourea administration, after right thyroidectomy, produced thyroid hyperplasia in rabbits, although large quantities of iodine were given simultaneously. An analysis of total iodine and thyroxine iodine showed a rapid decrease under these conditions; this iodine had been promptly excreted in the urine. The conclusion arrived at by the authors is that the inhibition of thyroxine formation indicates that thiourea produces a functional thyrostatic of the thyroid cells. Thiourea does not combine with iodine in the body. The cellular hyperplasia is associated with functional hyposecretion, the former depending on the stimulation of thyroid cell growth through the thyrotropic hormone. The site of action of thiourea is postulated to be in the thyroid cells, for if the drug merely combined with the iodine available, so preventing thyroxine formation, the goitrogenic action could be prevented by the administration of a sufficient dosage of iodine.

Yohimbine

Effect in posterior pituitary gland

Fugo describes investigations made in order to show that the antidiuretic effect of the alkaloid yohimbine is due to stimulation of the posterior lobe of the pituitary gland, which causes the release of larger amounts of its antidiuretic hormone. The experiments were made on female dogs of mixed breeds, the weight of which ranged from 6 to 16 kilograms, in 3 groups: (1) normal dogs; (2) dogs with diabetes insipidus, caused by section of the hypothalamic stalk; (3) normal dogs which were later completely hypophysectomized. The yohimbine was given in doses of 2 milligrams per kilogram of body weight, 1-3 times a day, for from one to 3 days as required for the experiment. In normal dogs yohimbine was found to produce an antidiuretic effect which was assumed to be due to the release of an antidiuretic principle by the posterior lobe. When administered to dogs with transected posterior lobes or completely hypophysectomized, yohimbine does not relieve the polyuria; on the contrary, the increased urine volume in the diabetes insipidus animals suggests the release of a diuretic principle from the anterior lobe. Completely hypophysectomized dogs showed no significant change in urine volume.

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PHYSICAL MEDICINE

Hyperthermy

Associated dangers

Etter analyses the published fatalities which have occurred after therapeutic hyperpyrexia and describes the minor discomforts of the measure. He uses a radiant heat cabinet. Petechial haemorrhages, circulatory collapse and heatstroke emerge as the causes of death. Hyperpyrexia, anoxia, hepatic damage and resultant prothrombin deficiency constitute the sequence which promotes haemorrhages; they occur submucously, in the endocardium and throughout the brain. Massive haemorrhages, gastric and intestinal, occur. The anoxia has a threefold origin. The increased temperature of the blood decreases the oxygen saturation and increases metabolism; this involves magnified oxygen consumption. Finally the deep respiration incidental to hyperpyrexia involves exaggerated expiration of carbon dioxide and raises the hydrogen ion concentration of the blood. This alkalinity entails a significant reduction of the arterial oxygen tension. Anoxia causes depletion of glycogen, which results in hepatic damage with depressed prothrombin and fibrinogen output, and these predispose to haemorrhage. These changes and their fatal outcome are delayed until the temperature has been normal over a period of many hours. From these findings it is deduced that preparatory to treatment the administration of dextrose in order to build up glycogen would be judicious, and that individuals suffering from hepatic disorder are unsuited to therapeutic hyperpyrexia. The necessity for routine oxygen administration, preferably by nasal catheter, is stressed and has been clinically demonstrated. During treatment the occasional emergencies are cerebral oedema, circulatory failure and heatstroke. If the circumoral pallor, tremor and explosive sickness which herald cerebral oedema yield to the intravenous administration of 100 cubic centimetres of 50 per cent dextrose and sucrose, treatment may continue, but coma or delirium requires its termination, as does circulatory failure from dehydration unless this

yields readily to dextrose and saline infusion. Pressor drugs are contra-indicated. In heat-stroke from derangement of the thermotactic centre the patient is removed from the cabinet and cooled by means of a fan and of tepid sponging. Of minor discomforts, apprehension yields to opiates and vomiting to saline infusion. Facial herpes, if not prevented by olive oil inunction, is mitigated by compound tincture of benzoin.

Hypothermy

Methods of application

Physiological and clinical observations.—Lowered metabolism occasioned by the application of cold has been found greatly to influence tissue survival, especially when there was impairment of the primary circulation. Newman states that cold is valuable in the production of anaesthesia for amputations, in the treatment of casualties of war and industry and in the treatment of peripheral vascular disease. Cracked ice, snow ice or iced water in rubber containers or in pails can be applied directly to the skin surface. Gordon's refrigeration box is useful and so is an apparatus with a thermostat that can be plugged into the house electrical system. A tourniquet should be adjusted and the cold applied for half an hour. Operations conducted under hypothermal anaesthesia are painless, except occasionally when the sciatic nerve is severed. Cold application to the stump is continued for 3 days. The absence of shock, pain and oedema and the inhibition of infection under this treatment is noteworthy. As healing is slowed the removal of sutures is delayed. In 15 cases of skin grafting, ice bags applied to the donor site for 2 hours gave complete anaesthesia for removal of grafts. In casualties of war and industry such as infected compound fractures, burns of extremities and crushing accidents, the application of cold controls haemorrhage, infection, shock and pain. In frost-bite and immersion foot there is tissue devitalization and anoxia. Treatment by refrigeration minimizes oxygen requirements. Transference to room temperature requires to be carried out gradually over a period of several days. It has been indicated by one worker that anoxia due to peripheral arterial disease with or without gangrene, to thrombosis or to embolism, is relieved when the surrounding temperature is low. In order to relieve the pain of cancer cold application has been prolonged for a period of 2 months without damage to normal tissue. In the treatment of burns experiments on animals showed that 75° F. is the most favourable environmental temperature for recovery. Since vasoconstriction is Nature's reaction to shock, treatment by the application of heat, which causes vasodilatation, needs revision.

Mechanotherapy

Exercise

Rehabilitation after abdominal operations.—For rehabilitation after abdominal operations, according to Shorter, not only medical or surgical skill is required but also collaboration of surgeon, physiotherapist, general practitioner and nursing staff. Before operation, save in emergencies, rehearsal of movements subsequently to be expected should begin, with exercises in breathing and coughing; smoking should be prohibited. In the author's plan of treatment, on the first days after operation the exercises are resumed, with manual pressure over the wound and assurance to the patient that the stitches will not burst. Retraction of the abdominal wall is practised on the second or third day unless such movement is contra-indicated. On the next day the exercises are repeated with fuller abdominal contractions and the addition of hip, knee, ankle and toe movements. On the fifth day movements of head and arms are added. On the sixth and seventh days flexion, extension and rotation of the trunk and arching of the back and legs are practised. Exercises from the eighth to the fourteenth day are repeated thrice daily, avoiding the occurrence of fatigue. Most patients are fit for discharge within a week of getting up. Patients who have undergone appendicectomy by muscle-splitting methods are allowed out of bed on the tenth day, and on the seventeenth those who have had herniotomy and paramedian laparotomy. On the first day up, when the slight giddiness has passed, such patients are taught difficult walking and balancing exercises. On the second day they join a convalescent class in the gymnasium for exercises and games, deck quoits being suitable and popular. After a week table tennis and long walks and runs prepare them for discharge; at the end of another fortnight they are seen again and are usually pronounced to be fit for work. By these means, physically the chest is cleared, thrombosis and embolism are discounted, and muscle tone and joint flexibility are maintained; mentally tedium is avoided and morale is promoted.

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PINTA

See also B.E.M.P., Vol. IX, p. 608; and Cumulative Supplement, Key No. 1262.

Clinical picture

Late stages

Pinta or carate is a contagious non-venereal disease endemic in lands and islands east, south and west of the Gulf of Mexico. Lieberthal describes 3 cases which occurred in parts of the United States of America hitherto believed to be immune. The causative organism is

Treponema carateum. The primary lesion is a non-ulcerating papule which develops at the site of the organism's entrance within from 7 to 20 days after infection. Secondary lesions, denominated pintids—in Mexico, empeines—appear from 5 to 12 months later around the primary lesion. These pintids imitate the eruptions of psoriasis, syphilis, trichophytosis, lichen planus or eczema; in Cuba follicular keratosis is frequent. In white patients, who are rarely affected, the lesions are pink or brown and in dark races they are purple, slate-coloured or black. During this secondary stage, which lasts for over a year, 60 per cent only of patients show a positive Wassermann or Kahn reaction. General health is unaffected. The lymphatic glands are sometimes enlarged in the late secondary and tertiary stages. Disturbances of pigmentation characterize the tertiary stage. The lesions are symmetrical, are usually in the extremities and consist of alternate areas of bleached and of exaggeratedly pigmented skin, the colour of which varies from light brown in white subjects to jet black in dark races. The mucous membranes may be involved. Cardiovascular degeneration, hypertension, aortitis or aneurysm accompany the later stages of the disease and changes in the spinal fluid have been discovered which resemble those found in cerebrospinal syphilis although clinical manifestations of neurosyphilis were absent. The cutaneous symptoms yield to anti-syphilitic treatment but cure by serological standards is tardy or unattainable. Pinta is not hereditarily transmissible.

Liebertal, E. P. (1943) *J. Amer. med. Ass.*, **123**, 619.

PITUITARY GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 611.

General clinical picture

Endocrine symptoms

Associated with renal insufficiency.—A case reported on by Beaumont and Robertson showed features of hypothyroidism secondary to pituitary deficiency, and of renal insufficiency. A woman aged 26 years had begun at the age of 19 to have attacks of abdominal discomfort, diarrhoea, thirst, oliguria and swelling of the legs, face and wrists. Cramps and tetany appeared at the age of 25 and twice coma developed, which lasted on one occasion for 7 days. Physical examination was negative. Although the renal function was only 25 per cent of normal the urine did not show casts and there was only an occasional trace of albumin. A radiograph of the pituitary fossa was normal. The insulin tolerance curve showed hypoglycaemia unresponsiveness, typical of hypofunction of the pituitary gland. Administration of thyroid extract caused signs of adrenocortical failure but when it was combined with sodium chloride, desoxycorticosterone and pregnant mares' serum the clinical condition improved and renal function became normal.

Beaumont, G. E., and Robertson, J. D. (1943) *Brit. med. J.*, **2**, 356.

PITYRIASIS RUBRA PILARIS

See also B.E.M.P., Vol. IX, p. 636.

Treatment

Carotene and vitamin A

Effects on dark adaptation and on the skin.—The effects of the administration of carotene and vitamin A to a mother who had inherited pityriasis rubra pilaris and to her 4 children were studied by Weiner and Levin. The thresholds of dark adaptation were raised in each case, as determined by biophotometer. An entirely satisfactory method for determining dark adaptation does not yet exist. The blood values for carotene and vitamin A in the family were followed by Clausen and McCoord's method, the photoelectric colorimeter not being then available. In each case the preliminary blood levels were within normal limits. Ingestion of vitamin A raised the blood content of vitamin A but not of carotene. When carotene was ingested the converse obtained. Neither lowered the dark adaptation threshold. The correlation of vitamin blood levels, dark adaptation and successful treatment has not yet been determined. The pityriasis dated in all cases from the first year of age and improved spontaneously in summer. In the mother, daily ingestion of 50,000 equivalent units of carotene produced in a month carotene discoloration and diminution of the follicular keratoses on the extensor aspects of the limbs but the extensor psoriasis-like plaques and the keratotic plugs on the dorsal aspects of hands and feet were unalleviated. Substitution of vitamin A up to 200,000 units daily within 7 months reduced all lesions to a faint erythema except for a surprising recrudescence of follicular keratosis. Cessation of treatment brought on a recurrence of the disease, which was controlled by resumption of administration of vitamin A with the successful addition of carotene for the keratosis pilaris. Comparable success with carotene in patients with keratosis pilaris unassociated with pityriasis was unobtainable. The children showed similar results. Apparently treatment must continue indefinitely.

Weiner, A. L., and Levin, A. A. (1943) *Arch. Derm. Syph.*, N. Y., **48**, 288.

PLACENTA: DEVELOPMENT AND DISEASES

See also B.E.M.P., Vol. IX, p. 641.

Abnormalities*Calcification of the placenta*

Report of a case.—Calcification in the placenta, although it is a degenerative process, is not a pathological condition. Thomas, who reports on a case, states that usually it does not involve foetal or maternal disease. Calcification occurs in the trophoblast or maternal side of the placenta in a reticular pattern. The amount of deposit depends upon the duration of pregnancy and the calcium metabolism of the mother. The obstetrician has commented on the phenomenon much oftener than has the radiologist since in X-ray examination foetal movements, uterine contractions and pulsation transmitted from the aorta and uterine vessels have obscured the minute and diffuse deposits. It is to be expected that the condition will be seen more often with use of the rotating anode tube. Thomas's patient was first seen during the fifth month of pregnancy and displayed dental disease only, indicative of disturbed calcium metabolism. A month before delivery and owing to irregular bleeding radiograms were taken to determine whether in fact there was a condition of placenta praevia. Normal labour however terminated a prolonged gestation estimated to have lasted for 324 days; the exact date of conception was rendered doubtful by earlier irregular bleedings. Such prolongation bears out previous observations that calcification is proportional to the duration of pregnancy. In suspected placenta praevia its exact implantation may be determinable skiagraphically by the reticular pattern and thereby the necessity for employing the elaborate procedures of iodide or air cystography may be obviated.

Thomas, S. (1943) *Radiology*, **41**, 573.

PLAGUE

See also B.E.M.P., Vol. IX, p. 675; Interim Supplement, No. 19*; and Cumulative Supplement, Key No. 1276.

Epidemiology*Rodents and fleas and the spread of plague*

Fleas and silvatic plague.—The importance of latent silvatic plague in relation to human bubonic plague is emphasized by Meyer, Holdenried, Burroughs and Jawetz. The authors have carried out during the last 3 years a study of the ground squirrel (*Citellus beecheyi*) population of the Calaveras Reservoir in California, among which plague was known to have occurred. In June 1942 it was noticed that a smaller number of squirrels were present in one district than at the corresponding season in the two previous years. Plague had not been discovered in squirrels which had previously been caught here and killed, nor in 'pools' of fleas removed from these and other rodents in the area. Inoculation experiments showed, however, that squirrels from this district possessed a greater degree of immunity than those from a supposedly non-infected area, and further investigations were undertaken. During June 1942, 99 squirrels were trapped and about 2,400 fleas, nearly half the number of which were of the species *Diplospilus montanus*, were collected from them. The fleas were placed in normal sterile saline with gentian violet 1 in 70,000 and kept in the refrigerator. When the collection was complete they were divided into 11 pools each containing from 110 to 280 fleas. Each pool was triturated in a mortar with a little salt solution and the suspensions were injected into guinea-pigs. Of the 11 pools 8 produced typical fatal plague infections. Field surveys and examination of burrows did not reveal any evidence of active infection of squirrels, and 376 necropsies did not show any sign of plague lesions; nevertheless inoculation of guinea-pigs with the pulped organs of 440 animals divided into 94 pools showed that 15 of the pools contained virulent organisms. Similar tests carried out later in the year gave results indicating that the epizootic of latent or occult plague came to an end late in August.

Meyer, K. F., Holdenried, R., Burroughs, A. L., and Jawetz, E. (1943) *J. Infect. Dis.*, **73**, 144.

PNEUMONIA, LOBAR

See also B.E.M.P., Vol. IX, p. 713; and Cumulative Supplement, Key No. 1279.

Diagnosis and differential diagnosis*Laboratory methods*

Lipid pneumonia and biopsy.—In almost every reported instance of lipid pneumonia the final diagnosis has been made on necropsy material. Nathanson, Frenkel and Jacobi suggest a biopsy of aspirated lung tissue as a diagnostic procedure in suspected cases. They were successful in corroborating the clinical suggestion in 5 out of 10 cases. The procedure is performed along usual lines and the material examined for characteristic lipid macrophages. The histological reaction to droplets of liquid paraffin entering the alveolar spaces are described. Some monocyte cells appear and phagocytose the oil droplets. At first these cells take on a foamy appearance but later in the course of imbibition they resemble ordinary fat cells; they then become bulky and irregular in contour. The nucleus is pushed to one side but eventually the cell disintegrates and giant cells and fibrosis appear as a response to the presence of a foreign body. At this stage the oil may be found entrapped in the meshwork of the fibrous tissue. If the amount of fat is considerable and the fibrosis and giant-cell formation so abundant as to form a tumour, the condition is referred to as a paraffinoma. Since the

aspiration of oil usually extends over a considerable period of time all stages are to be found on aspiration and at necropsy.

Treatment

Non-specific

Sulphadiazine used with and without antipneumococcus serum.—Shackman and Bullowa report the results of treating with sulphadiazine 232 patients with pneumococcal pneumonia. The gross mortality was 13·4 per cent or, excluding those moribund on admission who died within 24 hours, 8·3 per cent. Seventy of the more severely affected patients received in addition type-specific rabbit antipneumococcus serum. In the latter group the gross mortality was 14·3 per cent. There was a significantly greater death rate in patients over 40 years of age. The drug, which is the pyrimidine analogue of sulphapyridine, is said to be less toxic than the latter or than sulphathiazole and is more easily absorbed. Approximately 65 per cent of the drug given can be recovered from the urine; about one-third of this is conjugated. It is said however to be only one-quarter as effective against pneumococci in tissue cultures as is sulphapyridine or sulphathiazole in equivalent concentrations. It is suggested that a total dosage of from 10 to 24 grammes is adequate for two-thirds of the number of patients with pneumococcal pneumonias. An initial dose of 4 or 5 grammes was usually given, followed by 1 gramme every 4 or 6 hours until the temperature had fallen and had remained below 100° F., with a pulse rate below 90 per minute, for from 18 to 24 hours; the drug was then discontinued. The largest number of patients who recovered had a maximum concentration of 8·7 milligrams of the drug per 100 cubic centimetres of blood. Thirty-four patients had a secondary rise of temperature after discontinuance of the drug and 7 of these had more than one recurrence of fever, the temperature being normal between each recurrence. The presence of a detectable specific soluble substance, capsular carbohydrate or polysaccharide, in the blood was found to be of grave import. This substance is produced more abundantly by pneumococcus type III than by other types. Twenty-nine patients, of whom 2 died, yielded positive blood cultures. Antipneumococcus serum appeared to reduce the death rate in these bacteraemic cases. As regards toxæmia symptoms 7·6 per cent of patients had some nausea or vomiting. Gross or microscopical haematuria was not noticed but crystals were often found in the urine. Since the preparation of the report numerous other reports have appeared concerning renal damage—in at least one case fatal—caused by sulphadiazine. The problem is under further investigation by the authors.

Sulphamethazine and sulphadiazine compared.—Morgan and Wylie-Smith recount an investigation recently made by them into the relative efficacy and toxicity of sulphamethazine and sulphadiazine in the treatment of lobar pneumonia. Alternate cases of a series of 137 patients with true lobar pneumonia were treated, in order of admission, with either of the two compounds and the results obtained were contrasted with those of 354 cases treated with sulphapyridine. Sulphamethazine, the 4 : 6-dimethylpyrimidine compound of sulphanilamide, had been recently prepared by Rose and his colleagues, and preliminary clinical trials seemed to show it to be of high therapeutic efficacy and low toxicity. All 3 compounds were given in doses of 4 grammes to begin with, followed by 1 gramme 4-hourly, the maximum total dose in the case of sulphamethazine and sulphadiazine being 20–25 grammes, whereas a few of the sulphapyridine cases received as much as 35 grammes. In all cases a large fluid intake was ensured. The curative effect of sulphamethazine was found to equal that of sulphadiazine, and both compounds compared favourably in that respect with sulphapyridine. The incidence of toxic effects was 6 and 7 per cent respectively in the case of the first two compounds as against 52 per cent in the case of sulphapyridine. None of the cases treated with sulphamethazine or sulphadiazine developed oliguria or showed gastro-intestinal symptoms, but during convalescence there was a greater tendency for pleural effusion to occur than when sulphapyridine had been used. The temperature fell more rapidly with sulphapyridine, the average time being 29 hours, as against 43 and 35 hours in the case of the other two compounds.

Morgan, T. N., and Wylie-Smith, R. (1943) *Lancet*, 2, 731.

Nathanson, L., Frenkel, D., and Jacobi, M. (1943) *Arch. intern. Med.*, 72, 627.

Shackman, N. H., and Bullowa, J. G. M. (1943) *Arch. intern. Med.*, 72, 329.

POLIOMYELITIS AND POLIOENCEPHALITIS

See also B.E.M.P., Vol. X, p. 12; Interim Supplement, No. 13*; and Cumulative Supplement, Key No. 1282.

Aetiology

Experimental disease in animals

Proof of existence of virus in the intestine of the fly.—Rendtorff and Francis investigated the experimental infection of the house-fly with the Lansing strain of mouse-adapted poliomyelitis virus. It was found that in a single case under laboratory conditions the virus persisted for from 25 hours to 49 hours after ingestion by the house fly. It would appear that the virus is resident in the abdominal cavity and its disappearance is best explained as due to rapid excretion in the faecal and vomit spots; the latter are probably the mechanisms whereby flies spread the poliomyelitis virus. Tests made up to 20 days after feeding showed no recovery

of the virus after 49 hours, so that there is not any evidence of a secondary incubation period or of a multiplication of virus. The flies were kept in separate groups at temperatures of 25°, 30° and 35° C. and were equally infectious at any given period, showing that apparently this range of temperature has little or no effect upon the behaviour of the virus within the *Musca domestica*. Active poliomyelitis virus was recovered from a pooled suspension of faecal and vomit spots deposited during the first and the sixth hours after feeding. The virus could be detected in the abdomens but not in the heads and thoraces of the flies. It is concluded that the virus resides in the gastro-intestinal tract rather than on the exterior of the fly.

Immunity and resistance

Typhoid-paratyphoid immunization and poliomyelitis

Results of experiments on monkeys.—Earlier experiments for the purpose of investigating the reactions to poliomyelitis virus of animals immunized with typhoid-paratyphoid vaccine were vitiated by the intervention of rickets during immunization. Toomey and Tischer then selected 3 groups, each of 4 monkeys. Groups (1) and (2) during March and April received a diet rich in vitamins to which thiamine, carotene and viosterol were added. Simultaneously group (1) was immunized with 6 doses of a standard typhoid-paratyphoid A and B vaccine. Group (2) was not immunized. At mid-May groups (1) and (2) received a subcutaneous inoculation of poliomyelitis virus. The dose was 70 cubic centimetres of a 10 per cent suspension of pooled unpurified monkey's cord diluted in typhoid-paratyphoid colon bacillus filtrate (enteric toxin). Group (3) received 0.5 cubic centimetre of the preparation intracerebrally. All animals acquired poliomyelitis. Group (1) acquired a fulminating disease and the animals died within 5 days. Necropsy showed advanced destruction of the anterior cornua and lesions which resembled the post-mortem appearances described in human beings who die of fulminating poliomyelitis. In group (2) localized paresis developed without severe illness. When the animals were killed after 3 weeks, pathological changes resembling those in group (1) were evident in lesser degree although they transcended the clinical picture. Group (3) displayed quadriplegia within 8 days without severe indisposition. When the monkeys were destroyed, pathological changes resembling those in group (1) were observable. It emerges first from the earlier and the second investigation that typhoid-paratyphoid immunized animals, rachitic or not, are more susceptible to poliomyelitis than are non-immunized animals. Secondly—and this is supported by other experiments—it was found that in animals fed with vitamin D a factor exists inimical to the spread of poliomyelitis virus. Efficient myelin formation may be this factor, since myelin is known to deteriorate during vitamin D deficiency.

Clinical picture

Associated arthritis

Distinguishing features.—Poynton utilizes the report on an epidemic of anterior poliomyelitis to illustrate its long known but not widely recognized form of arthritis. The swelling is mono-arthritic, painful at onset, not reddened but sometimes heated and affecting usually ankle, knee, hip, elbow or wrist. It occurs before or despite treatment and, persisting sometimes for months, ends usually in recovery, occasionally in fibrous ankylosis. Palpation suggests at first a distended and later a thickened capsule. Radiography confirms this and shows rarefaction of bone. There is never suppuration and pyrexia does not accompany an arthritis remote from the onset of poliomyelitis. Usually a limb severely paralysed is selected; unparalysed limbs are probably immune. As in Charcot's joints, nervous destruction may be the condition responsible for the arthritis but virus infection, as in the arthritis of dengue or mumps, is the more probable factor. The view receives support from general symptoms such as irritability and mental fatigue, with localized sweating and moist hands reminiscent of chorea and rheumatoid arthritis. The notable localized sweating led the nursing staff to classify their patients as wet or dry cases. Rheumatic fever, tuberculous arthritis, osteomyelitis involving a joint and meningococcal arthritis may cause confusion when paralysis is slight. Distinguishing features are the muscular wasting and static blood sedimentation rate in poliomyelitis and the rapid rise in sedimentation rate supplemented by cardiac manifestations in rheumatic fever and the results of tuberculin tests in tuberculous arthritis. Osteomyelitis displays altered blood sedimentation rate, undermined cartilage (shown by radiography) and damage to the bone shaft. Examination of the cerebrospinal fluid helps to differentiate poliomyelitis from meningococcal infection. Immobilization of the joint, sometimes assisted by the gentle pressure of careful strapping, is the required treatment.

Treatment

The paralysis

The Chicago epidemic of 1943.—In poliomyelitis the incidence of bulbar involvement, the severity of paralyses and the mortality vary widely with the epidemic rather than the treatment. Sherman illustrates the natural course of anterior poliomyelitis by a study of 70 patients in the Chicago epidemic of 1943. The sexes were approximately equal, with 42 patients under and 28 over 10 years of age. Bulbar and bulbosplinal involvement each affected 9 patients, spinal paralysis affected 39 and 13 patients were non-paralytic. Hitherto the omission of non-paralytic and abortive cases has vitiated statistics. Spinal puncture was usually employed together with absolute rest and approximately normal diet supplemented when necessary by fluid given parenterally. For bulbar patients constant suction and oxygen by nasal catheter

were utilized and all nourishment was administered parenterally. Intercostal weakness in 3 cases necessitated the use of the respirator. Early activity for all was encouraged and physiotherapists supervised the exercises of 7 patients with severe weakness who will ultimately require the aid of braces or of surgery. Of the remainder, 13 were never paralysed, 44 are now capable of normal life with or without some degree of weakness and 6 died. Convalescent serum appeared to be ineffective. The Kenny system was not employed.

Kenny concepts and treatment.—Gill analyses the Kenny concepts and treatment of infantile paralysis. Sister Kenny claims that the flaccid muscles are really normal, and that loss of ability to contract these is due to functional dissociation (alienation) from the nervous system. Ability to contract the non-functioning muscles returns only after releasing spasm in the opponents and although true paralysis due to nerve cell death does occur uncommonly, the supposed weakness is due to untreated spasm and to disuse of the dissociated muscles. In short, physiological function of the nervous system is disturbed and is of greater importance than actual architectural damage. Muscle spasm rather than paralysis is the primary lesion. Incoordination is the third of Miss Kenny's postulates. Muscular spasm, however, has long been recognized as a feature of poliomyelitis and its origin is reflex and not, as Kenny claims, due to inflammation of the muscle. Gill states that the existence of the latter state is unconfirmed and he is unable to view the flaccid paralysis as evidence of anything other than motor cell destruction. Rest and heat have always been the orthodox methods in the presence of inflammation and in this orthodox principles do not differ in any way from those formulated by Kenny. The latter stress the avoidance of any form of immobilization, which Gill considers to be contradictory to the necessity she emphasizes of avoidance of overstretching of paralysed muscles. The Kenny concept of the value of hot packs is dependent upon the assumption of an inflammation of the muscles themselves, which assumption is incorrect. In the stage of convalescence, when muscle tenderness has disappeared, active and passive movements are begun; Gill concludes that the Kenny and orthodox methods at this stage are similar, the one distinctive feature in the former being the use of the hot pack to relieve spasm. The author believes that 'the Kenny furor will eventually subside'.

Comparison of the Kenny system with previous methods.—Rechtman, in differentiating the orthodox treatment of infantile paralysis from the inadequate methods of the past, states that Miss Kenny's criticisms apply rather to the inadequacies than to orthodox methods properly applied. Orthodoxy bases treatment on pathology. Partial and temporary derangement of the anterior horn cells gives hope of recovery, but destruction entails paralysis of the muscles involved. Such paralysis is displayed in 20 per cent of cases. Miss Kenny admits the existence of 10 per cent of true paralysis but does not acknowledge a condition to be established until adequate treatment for a period of 2 years has failed. Formerly she denied its existence, her theory of the disease being based less on pathology than on the effect of muscle spasm, muscular incoordination and mental alienation. Orthodox treatment employs the Bradford frame, the scultetus binder and later the Hoke corset and the Toronto splint which gives place later to the airplane splint. Plaster splints are used for weakness below the knee. Heat, hydrotherapy and gentle massage afford comfort and are all applied with minimum handling of the patient. Joints are early moved through their painless range. The positions of sitting and standing and the exercise of walking, with leg or ankle brace in affections of the leg, accompany the return of muscular power. The first target of the Kenny system is relaxation of spasm. Intensive heat, notably by the application of fomentations, is employed, splinting is disapproved of and even in respiratory embarrassment heat displaces the respirator. The flaccid muscle cannot function because of spasm in an opposing muscle and the central nervous system ceases to communicate with the nervous arc controlling the flaccid muscle. This is 'mental alienation'. Simultaneously incoordination and muscle substitution occur. For the correction of these, muscular re-education is early instituted by the Kenny treatment.

Reasons for preferring the orthodox treatment of poliomyelitis to the Kenny treatment are discussed by Key. Both methods are described and the writer points out that the Kenny method does not even claim to give a higher percentage of cures. Advocates of the Kenny method however state that the orthodox treatment is based on wrong principles because the true symptoms of the disease were not recognized until Miss Kenny discovered them. The author maintains that Miss Kenny's concept of the disease is not new and that her contribution to the symptomatology is the giving of new names to well known symptoms all of which have been recognized and treated by orthodox methods. The orthodox treatment is elastic and can be varied to suit individual patients; it also takes into account the natural tendency of the muscles to recover their function spontaneously. In the Kenny method no account at all is taken of spontaneous recovery but all recovery is attributed to the treatment used. Braces are prohibited and it is even claimed that the board at the foot of the bed is not used for the purpose of preventing equinus of the feet but in order to stimulate the normal standing reflex. Patients are not permitted to sit up or to walk nor are they allowed out of bed until muscle spasm has disappeared. Paralytic patients are thus kept flat in bed month after month and are treated by hot packs and muscle re-education. The Kenny treatment is wrong in theory because it supposes that the main lesion of the disease is spastic contracture due to an acute inflammatory disease of the muscles. The orthodox treatment recognizes that the principle lesion is in the anterior horn cells of the spinal cord, and that the chief cause of crippling (if deformities are prevented) is the permanent weakening of flaccid paralysis of muscles the

anterior horn cells of which have been partially or completely destroyed. It prevents deformities, protects paralyzed muscles and restores the maximum amount of power to all the muscles which retain some nerve supply.

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PREGNANCY: NORMAL AND PATHOLOGICAL

See also B.E.M.P., Vol. X, p. 48; Interim Supplement, No. 18*; and Cumulative Supplement, Key Nos. 1291-1303.

Physiology

Alimentary system

Morning sickness.—Reynolds regards the vomiting of early pregnancy and indigestion later as stages of one condition which lacks a universal explanation. Neurotic patients suffer most but not exclusively. Administration of sugar often brings relief but carbohydrate deficiency is not proved and neither is vitamin deficiency nor toxæmia. Endocrine disturbance seems plausible but this theory has not illuminated treatment. In the management of morning sickness attention first concentrates on outdoor exercise with avoidance of fatigue, and on diet. Walking is best, cycling until it causes discomfort is harmless. Tennis, golf and riding must be the patient's responsibility as they entail some risk. Senna pods or salines and less hurry secure the essential free evacuation without residuum. Meals should be small and taken often; the diet should include glucose and a pint of milk, with avoidance of fatty foods and pastries. Biscuits and tea on waking may be helpful. Late rising is discouraged but postprandial rest is beneficial. Uterine retroversion may need correction or a grumbling appendix may require removal. If alkalis fail, weekly or semi-weekly injection of oestrin (for instance progynon) is the next resort and if this is unsuccessful a suprarenal extract such as eucortone may be tried, or finally intravenous injection of glucose, if necessary combined with insulin. Confinement to bed remains to be tried, with termination of pregnancy as a last resort. Indigestion later in pregnancy includes heartburn, nausea, flatulence and retrosternal or epigastric pain; the last two symptoms combined with palpitation or dyspnoea are danger signals. Pregnancy must not be allowed to mask gastric and cardiac lesions or ureteral calculus, pneumonia and gall-stones. In treating heartburn alkalis often succeed and dilute acids do so equally often. Severe cases require 0.0005 gramme of prostigmin given intramuscularly once a week. Nausea may yield to three doses of calomel, $\frac{1}{2}$ of a grain after meals, followed by Epsom salts next morning; this treatment should be repeated at intervals. In flatulence acids, alkalis, sal volatile and belladonna are useful. For sleeplessness causing or resulting from indigestion, luminal given by day avoids the undesirable suggestion of a hypnotic.

Changes in the maternal organs during pregnancy

Implantation hæmorrhage.—Impending eclampsia compelled the induction of labour in a mother of 5 living children. Studdiford describes the contents of the uterus removed when, although warned of the danger, she again became pregnant. The description illuminates the time relation between ovulation and fertilization and the occasional bleeding accompanying the implantation of the ovum. The last menstruation occurred on 18th August, 1942 and hysterectomy was performed on 25th September. Comparison with a monkey embryo dated the specimen at 26½ days. Taking 31st August as the day of fertilization, this date coincides with the onset of that part of the menstrual cycle when ovulation is believed usually to occur. Interest next centres in the degenerative and hæmorrhagic changes microscopically observed in the decidua capsularis. This early degeneration appears contingent upon the stretching and attenuation of the layer of decidua between the maternal blood space and the uterine cavity, not upon lack of progesterone stimulation. Implantation of the ovum may be accompanied by bleeding, usually slight. Persistence of these hæmorrhagic and degenerative changes may well account for the bleeding sometimes occurring during the first three months of otherwise normal pregnancies. Furthermore, rupture of this attenuated layer may lead to profuse hæmorrhage which will terminate pregnancy unless the bleeding surface is promptly sealed by-clot. The sudden bright hæmorrhage in abortions of such origin contrasts with the brownish discharge preceding the abortion of a defective ovum.

Hyperemesis gravidarum

Treatment

By dieting and eserine sulphate.—Acting on the hypothesis that vomiting of pregnancy results from hyperactivity of the sympathetic nervous system with consequent depletion of liver and muscle glycogen and carbohydrate starvation, Turnbull has treated 31 patients with eserine sulphate in conjunction with a high carbohydrate diet. Eserine sulphate was chosen in preference to ergotamine because of the action of the latter drug upon the gravid uterus and the difficulty of determining the correct dose in view of the fact that small doses stimulate the

sympathetic system and of the possibility that large doses, which inhibit it, might be dangerous. Eserine sulphate was given in doses of $\frac{1}{1000}$ grain two or three times daily, according to the severity of the condition. The oral route was used unless the drug was vomited, in which case recourse was had to hypodermic injections. A tablespoonful of glucose in a glass of water flavoured with fruit juice was given 15 minutes afterwards. In 4 cases the treatment was interrupted on several occasions, but in the remaining 25 it was carried out regularly. In the 4 cases the average number of days after the first dose of eserine on which vomiting occurred was 12.75; in the others it was 3.83. Of the 31 patients only 2 failed to respond to the treatment and needed to have the pregnancy terminated. The author meets the objection that if deficiency of liver glycogen is the cause of vomiting of pregnancy the blood sugar level should be lowered, by pointing out that the blood sugar tends to remain within constant limits whatever the state of nutrition. In experiments conducted by the author eserine was found to produce an initial rise in the blood sugar level, sometimes followed by a fall. The suggestion is made that hypertension in pregnancy may be another manifestation of sympathicotonia.

Effects of pyridoxine hydrochloride.—Weinstein, Mitchell and Sustental describe their experiences with pyridoxine hydrochloride in the treatment of the nausea and vomiting of pregnancy. They have used the drug in 32 cases in doses of 50–100 milligrams 3 times a week by intramuscular injection. The maximum total dose was 1,050 milligrams. There were not any untoward reactions and in almost all cases the results were favourable and the response rapid. Of 16 patients with nausea present in the mornings only, 14 were completely relieved and 2 improved. Of 6 with nausea persisting throughout the day, all were completely relieved. Of 4 with nausea and occasional vomiting, 3 experienced complete and one slight relief. Of 6 with nausea and vomiting so severe that no food was retained, all were completely relieved. The authors believe that pyridoxine hydrochloride is a valuable remedy but should be used in conjunction with sedatives and a regulated diet.

Toxaemias of late pregnancy

Pre-eclamptic toxæmia and eclampsia

Cerebral atrophy as a sequel.—A case described by Lowenberg and Lossman illustrates the rare condition of cerebral atrophy occurring after eclampsia and probably caused by toxic influences. In the patient, a primipara of 20 years old, toxæmia of pregnancy developed 3 days before delivery. One hour after delivery she passed into *status eclampticus*; the convulsions persisted for 14 hours and coma for 60 hours. When she recovered consciousness mental deterioration was apparent. The patient had to be fed, paid no attention to her surroundings, did not speak and made no response to stimuli or questions. In this state she continued until her death 6 years later. Necropsy revealed chronic suppurative pyelonephritis, amyloid disease of the kidneys, liver, spleen and myocardium, an old tuberculous lesion in one lung and advanced cerebral atrophy. The brain weighed 579 grammes. It showed severe bilateral atrophy of the frontal, temporal and parietal lobes and of the thalamus, moderate atrophy of the precentral and postcentral gyri, the occipital lobes and the caudate nucleus, putamen and pallidum, and slight atrophic changes in the pons and cerebellum. Sections revealed cystic degeneration of the white matter throughout the brain and of the gray matter also in parts of both temporal lobes and in the right frontal lobe.

Persistent hypertension after toxæmia of pregnancy

Rapid progress of the disease.—Nine cases of vascular disease in which the patient had hypertension after toxæmia of pregnancy are described by Golden, Dexter and Weiss. All but one of the patients were known to have been free from signs of cardiovascular or renal disease before or early in the pregnancy in question. The term, toxæmia in pregnancy, is here used to describe the appearance in the latter half of pregnancy of abnormal elevation of the blood pressure above the pre-pregnancy level, or an increase in albuminuria above the pre-pregnancy level with or without generalized oedema, and with rapid diminution of these abnormalities before or soon after delivery. In all the cases the duration rather than the severity of the toxæmia appeared to be the determining factor in the development of persistent hypertension. The authors, indeed, advocate termination of pregnancy when toxæmia fails to respond to treatment in 3 weeks. A long latent period often intervenes between the toxæmia and the appearance of hypertension; instances in which this latent period was as long as 5 years have been described, but as the authors point out it is impossible in such cases to decide whether or not other agents were at work in the interval and how far the toxæmia of pregnancy is responsible. In most patients, however, blood pressure and urinary findings never return to normal. Once established, post-toxæmic hypertension runs a course resembling that of other types of cardiovascular-renal disease, but tends to progress comparatively rapidly. Death usually results from uræmia, cardiac failure or cerebral haemorrhage. Histological examination of the kidney in 3 of the 9 cases showed that there were advanced sclerotic changes in the arterioles and destruction or hyaline degeneration of many of the glomeruli. Many of the tubules were atrophic. In a fourth case the tubules had borne the brunt of the attack and damage to the glomeruli was comparatively slight.

Diseases of the nervous system

Encephalitis epidemica

Report of a case.—A case of epidemic encephalitis which occurred during pregnancy is recorded by Hall, who points out that it is now well recognized that in such cases labour may be normal and the infant healthy. In the case reported the woman was 23 years old when she

first became pregnant. In the eighth month of pregnancy severe epidemic encephalitis developed. After a normal labour and the delivery of a healthy female child Parkinsonism developed and the patient was in bed for 18 months; she improved after treatment with belladonna. Sixteen years later she became pregnant again and gave birth to a normal boy, but there was absence of lactation due to the continued administration of belladonna during pregnancy. Subsequently the disability due to Parkinsonism increased. A daily dose of 1 drachm of tincture of belladonna during a period of 11 years, continued during pregnancy, apparently had no injurious effect on the second child.

Diseases of the endocrine system

Diabetes mellitus

Effect on the foetus.—The cause of the great mortality of the foetus or the newborn offspring of mothers suffering from diabetes mellitus is obscure. Miller, Hurwitz and Kuder observed 137 diabetic mothers and their foetuses. They found from case histories that the foetal and neonatal mortality had been just as great in the 5 years preceding the onset of diabetic symptoms as it was after the appearance of diabetes. The fact that diabetic women give birth to large babies is well recognized. The foetal and neonatal mortality of large babies was found to be no greater than that of small babies. In the diabetic cases the foetal and neonatal mortality was about 5 times greater than in nondiabetic mothers. Women who have glycosuria, diabetic dextrose tolerance curves and much fasting blood sugar, but who do not need insulin, should be watched during pregnancy since the neonatal and foetal mortality is heavy in this group, as it is among mothers who have glycosuria but whose carbohydrate metabolism is otherwise within normal limits.

Pulmonary tuberculosis

Effect of pregnancy on tuberculosis

Report of a hundred cases.—In a paper on the effect of pregnancy and parturition on pulmonary tuberculosis, Cohen records the results of pregnancy and labour in 100 consecutive cases confined in the maternity unit of the Essex County Council Sanatorium at Black Notley. The cases were divided into 3 groups: (1) arrested and recovered cases which had shown no evidence of active disease for over 2 years, (2) quiescent cases and (3) progressive cases in which the patients showed evidence of active disease when admitted to hospital. Group (2) patients were usually admitted 6–8 weeks before confinement and lived an active sanatorium life. The progressive cases were given the appropriate sanatorium treatment, not excluding such active measures as collapse therapy, for the pulmonary condition. During labour forceps were not applied at the beginning of the second stage as a routine, but were used if the patient showed signs of fatigue after 2 hours. The anaesthetic used was chloroform or gas and oxygen. In 7 out of 25 progressive cases increased pulmonary disease was found, but out of 75 quiescent, arrested or recovered cases only 5 showed increase. All the 12 patients who showed increased pulmonary disease had normal labours. Forceps were used in 23 cases with no ill effects. From the 100 cases observed Cohen concludes that under favourable conditions, such as are found in a sanatorium, pregnancy and labour *per se* do not necessarily affect unfavourably the ordinary progress of pulmonary tuberculosis; therefore therapeutic abortion need not be undertaken as a routine although it may be necessary in cases of very active or very advanced disease.

Tumours complicating pregnancy

Fibromyomas of the uterus

Do fibroids enlarge during pregnancy?—Randall and Odell report some observations which cast doubt on the belief that fibroids enlarge during pregnancy. Fibroids removed from 17 pregnant women by hysterectomy or myomectomy showed no evidence of hypertrophy of muscle fibres and no hyperplasia of the connective tissue cells. Oedema of significant degree was present in only one of the tumours. Ten showed degenerative changes, that is, red degeneration. In none was increased vascularity apparent. These findings controvert all the theories advanced to account for the supposed enlargement of fibroids during pregnancy. These include hypertrophy of muscle, increase of connective tissue, oedema and vascular engorgement.

Ovarian tumours

Treatment of cysts by ovariectomy.—Normal delivery is not precluded by the presence of an ovarian cyst but on the other hand such a cyst is one of the most dangerous complications of pregnancy. Capone states that as the result of the presence of an ovarian cyst there may occur (1) abortion or premature labour, (2) obstructed delivery which will necessitate Caesarean section, (3) rupture of the cyst during delivery, (4) rupture of the uterus or (5) gangrene of the tumour after prolonged pressure. Analysis has shown that dermoids constitute 50 per cent of such cysts, that more than a quarter of the number of cysts occupy the true pelvis and that of these three-fifths are dermoids. Since the common occurrence of such a growth has been disputed, a case is cited which illustrates the rapid growth of a cyst during the patient's pregnancy. Here pregnancy (apart from a slight dyspnoea) and delivery at term proceeded normally, yet a cyst which contained 14 quarts of fluid was removed 8 days later. The case of another patient illustrated rupture of a dermoid cyst after difficult labour, with ensuing chemical peritonitis. The third case is that of a patient who had an abortion at 2 months due to cystic suppuration. Pregnancy complicated by ovarian cyst necessitates ovariectomy. Opera-

tion during the first 3 months is avoided lest possible removal of the corpus luteum should promote abortion. Diagnosis of a cyst in the last months of pregnancy offers two alternatives. By performing Caesarean section and ovariectomy at term the risk of subjecting a recent cicatrix to the strain of labour is avoided. Alternatively, if it is judged that labour will be normal it may be allowed to proceed, ovariectomy being postponed until the puerperium. An ovarian cyst detected during the puerperium should be removed without delay.

Cancer of the cervix

Important factors.—In the course of 30 years the Mayo Clinic admitted 3,570 patients with cervical carcinoma of whom 26 (0·7 per cent) were pregnant. Maino and Mussey analyse the carcinomatous cases with regard to incidence, prognosis, treatment and the occurrence of conception during established disease. These patients sought admission for disease. During the same period 8,500 women normally pregnant were observed. The ages of patients ranged from 25 to 41 years with an average of 32 years. Age influenced neither incidence nor prognosis, nor were these affected by the number of previous pregnancies, which averaged 6. Only once however did carcinoma occur in a first pregnancy. In one case curettage after abortion showed carcinoma, yet the patient again became pregnant, which proves that carcinoma may precede pregnancy. In 3 other cases this sequence was probable. Bleeding, trivial or profuse, was the first symptom in 88 per cent of cases and the average date of diagnosis was during the twenty-fourth week of pregnancy. The fear of causing abortion too often delays pelvic examination, but the authors agree with Rochet who states that even biopsy carries little risk. When the tumour is operable panhysterectomy is recommended for all cases, with post-operative irradiation. It is preceded by Caesarean section for viable infants. This procedure attained a 5-year freedom from recurrence in 57 per cent of cases. When the tumour is inoperable, irradiation is preceded by Caesarean section for the purpose of delivering a viable foetus; if the foetus is non-viable irradiation only is practised and the inevitable abortion is accepted. Operation with post-operative irradiation surpasses irradiation alone in cervical carcinoma of the pregnant (as contrasted with the non-pregnant) uterus. Nevertheless, the survival of one apparently hopeless case for 11 years after irradiation alone was noteworthy.

Venereal diseases

Syphilis

Need for antisyphilitic treatment early in pregnancy.—Dippel discusses the relation between congenital syphilis and abortion and miscarriage. He gives the results of the study of a series of 68 foetuses of non-syphilitic and 67 foetuses of syphilitic women; only those which had not reached viability were included. The diagnosis of foetal syphilis was made only on the findings of spirochaetes in foetal organs. Spirochaetes were not found in any of the 68 foetuses of non-syphilitic women. In the group of luetic women, no spirochaetes were found in 12 foetuses of ages ranging from the fourteenth to the seventeenth week of gestation. Roughly 10 per cent of the 29 foetuses of from the eighteenth to the twenty-second gestational week were infected. In the late miscarriage period the incidence was 50 per cent, with the highest rate (66·7 per cent) in the twenty-sixth week. There appeared to be some natural protection of the foetus against syphilis in the early weeks; probably Langhans's layer of chorionic epithelium affords this protection, even after the sixteenth week, when it may persist in the form of delayed delamination and differentiation of the Langhans cells. To protect their foetuses from infection, Wassermann positive mothers must be treated before the eighteenth week of gestation, and both Wassermann positive and Wassermann negative mothers must have treatment before the twenty-third week; otherwise approximately 50 per cent of their foetuses may be infected before viability is reached. These findings confirm the modern teaching that anti-syphilitic treatment must be started early in pregnancy.

Focal infections

Secondary exacerbation

Effect of infective foci on course of pregnancy and labour.—Various obstetrical observers consider that many of the complications and diseases associated with pregnancy and labour are due to pre-existing foci of infection in the body which may have remained dormant after an initial acute stage. Solis-Cohen gives an account of various conditions which may be caused by secondary focal infection. Abortion may in some cases be due to haematogenous infection with placental infarction. Toxaemia, toxic vomiting and eclamptic conditions may be related to bacterial invasion of organs and the elimination of infective foci has sometimes been curative. Many workers believe that in nephritis of pregnancy and in pyelitis, infection is an aetiological factor which should be sought. Premature separation of the placenta may be the result of thrombosis due to haematogenous infection, and in puerperal sepsis and in phlebitis internal focal infection should be recognized as being a possible source of danger. In some cases of breast abscess similar infecting organisms have been found to exist elsewhere in the body. During pregnancy attempts at removal of infective foci should be undertaken with great caution. Metastatic foci should never be eradicated; the production of antibodies should be stimulated by potent autogenous vaccines and sulphonamide therapy may be advisable.

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PROSTATE DISEASES

See also B.E.M.P., Vol. X, p. 146; and Cumulative Supplement, Key No. 1308.

Simple enlargement

Differential diagnosis

Importance of exhaustive examination.—Although the symptoms characteristic of prostatism arise commonly from disorders of the prostate, Lazarus states that their origin may be extraneous and the prostate may be normal. Further difficulty in diagnosis is encountered when the prostate although enlarged is not the source of the symptoms. Haematuria is first considered by Lazarus. When it is truly prostatic haematuria arises usually from ulceration of the mucosa which covers enlarged lateral lobes. In order to illustrate haematuria of extraneous origin cases are cited of renal neoplasm. Next comes for consideration the group of cases in which the prostate is enlarged but in which the haematuria is in fact due to one of its frequent concomitants, vesical tumours and calculi, or cystitis. In this group must be included the occult or visible haematuria of a concomitant nephritis, pyelonephritis or hydronephrosis. When obstruction arises from a median bar it should be remembered that the bar may be independent of the underlying hypertrophied prostate, the enucleation of which will therefore be ineffective. In prostatic enlargement the determination of acid phosphatase blood levels may decide a debatable malignancy. The interrelation of prostatic and intestinal symptoms demands careful investigation. The irritation of the rectal wall and the narrowing of the lumen which is usual in prostatic enlargement must not be allowed to mask the existence of a rectal neoplasm. Conversely, tenesmus and spasm which occur as a result of intestinal growth must be distinguished from similar symptoms caused by an enlarged prostate. The consideration of symptoms and the making of digital rectal examination alone are unreliable for the purpose of making a diagnosis. A careful case history, pyclography, ureteral catheterization and the use of the cystoscope and the sigmoidoscope are also necessary if grave error is to be avoided.

Treatment

Transurethral resection: post-operative investigations.—As the inventor of the original instrument for urethrosopic prostatic resection, Young speaks with peculiar authority when he condemns the indiscriminate use of this method in all types of prostatic obstruction and urges the importance of careful selection of cases. He states that encouraged by the results of transurethral resection for small bars and contractures at the vesical neck he himself extended its use in order to deal with larger and larger prostates, but as time went on he was forced to recognize that perineal enucleation was equally safe and was far more lasting in its results. Since then various workers have introduced modifications of the original procedure and thousands of cases have been reported. The conclusion emerges (1) that the operation is not entirely free from danger; (2) that convalescence is often prolonged; (3) that incontinence actually occurs more often than after the perineal operation, of which it has been regarded as one of the chief drawbacks; (4) that recurrence is common. Moreover, the presence of cancer may be missed. The author has now seen 200 patients who have sought advice after transurethral resection had been performed elsewhere. The cases are divisible into the following groups. (1) Benign hypertrophy in which prostatic lobes weighing from 50 to 100 grammes were enucleated by perineal prostatectomy; (2) benign hypertrophy in which the enucleated lobes weighed from 100 to 200 grammes; (3) benign hypertrophy in which the lobes weighed over 200 grammes; (4) benign hypertrophy with lobes weighing less than 50 grammes; (5) imperfect results but prostatectomy not indicated; (6) cancer too advanced for radical operation; (7) cancer in which radical operation seemed worth while. In all these cases symptoms had persisted or recurred after from one to 4 transurethral operations. Prostatic calculi were found in a number of the cases of benign enlargement, notably in 4 of the 19 patients included in group (4) above. In many patients severe prostatitis was present; it is certainly more common after transurethral resection than after perineal prostatectomy. Patients in group (5) numbered 87. Often their symptoms were due to severe infection of the bladder and urethra. Of the 26 patients with advanced cancer of the prostate 5 had had 2 and one had had 4 transurethral resections. Group (7) included 4 cases in which cancer had been

found on microscopical examination of tissue removed by transurethral resection and in which radical operation was performed. One patient died from metastases; the others are alive and well between 2 and 3 years after operation.

Malignant disease

Aetiology and morbid anatomy

Rare testicular lesion.—Sharnoff and Lisa report a case in which orchidectomy for prostatic carcinoma disclosed a rare and unsuspected lesion of the testis. The patient, aged 67 years, had a carcinoma of the prostate with metastases in the ribs, clavicles, scapulae, pelvis, vertebrae and femora. Bilateral orchidectomy was performed. When the testes were examined one of them was found to contain a nodule 4 millimetres in diameter which on section was found to be a tumour of the interstitial cells of Leydig. Its malignant character was inferred from the presence of hyperchromatism, mitoses and macronucleoli and from the variation in size of the nuclei.

Clinical picture and diagnosis

Early carcinoma.—Speaking to the Kansas City Southwest Clinical Society on the diagnosis and treatment of early carcinoma of the prostate, Henline made the following points. The cause of prostatic carcinoma is possibly an imbalance between the male and the female sex hormones, with preponderance of androgen. This endocrine imbalance is known at least to favour growth and metastasis. The prostate is originally composed of 5 lobes, anterior, posterior, median and two lateral. Normally only the two lateral lobes persist into adult life. Carcinoma, which is estimated to occur in 15 per cent of men over 50 years of age, usually develops in the vestiges of the posterior lobe, an area rarely if ever affected by hyperplasia or infection; it may arise however in any part of the gland. Symptoms are absent in early cases. A hard nodule felt per rectum is the only sign of early prostatic carcinoma. At this stage removal of the entire prostate will eradicate the disease. Spread outside the gland and metastasis are late phenomena. The only hope of discovering an early case lies in the fact that occurrence of other disorders of the prostate are common at the age at which carcinoma is apt to develop. These disorders are attended by symptoms which may bring the patient to the doctor and rectal examination may then reveal a suspiciously hard area, often giving the impression of having a 'square edge', in the posterior part of the gland. Such a finding justifies and demands perineal exploration and biopsy without delay. The author advises that frozen sections be made and that if they confirm the diagnosis complete prostatectomy with removal of the seminal vesicles be carried out forthwith. If the section fails to reveal carcinoma the wound is closed. Since the urethra has not been opened the patient can be discharged in a few days.

Phosphatase.—Gilbert and Margolis report on the following case. A man aged 46 years was admitted to hospital for progressive urinary obstruction which had been present for one year. The prostate was greatly enlarged by a mass extending beyond the limits of the gland. X-ray examination did not show any evidence of metastasis. Serum alkaline phosphatase was 3·8 units. Treatment consisted in transurethral resection followed by deep X-ray therapy. The resected tissue was histologically malignant. Serum alkaline phosphatase on discharge was 9 units. The patient was re-admitted 5 months later with clinical signs of metastases in the spine and pelvis and radiological evidence of metastases in the lungs. Serum alkaline phosphatase was 13·1. Castration was performed with prompt relief of pain. An X-ray examination 5 months later showed metastases in various bones but remarkable clearing of the lungs. The prostate was still larger than normal. Serum alkaline phosphatase was 11·7, acid phosphatase 3·5 units. Stilboestrol was given for 12 days with some relief. Acid phosphatase rose to 9·4. The patient was admitted in a moribund state 10 months after castration, with enlarged liver and serum acid phosphatase 42·5 units. An autopsy specimen of tumour tissue contained 8 units, as contrasted with an average for normal prostatic tissue of 1,199 units of acid phosphatase.

Treatment

Operative conditions.—Greene draws attention to the limitations of the commonly performed operations for benign prostatic hypertrophy, quoting 2 cases in which carcinoma of the prostate developed 17 years and 10 years respectively after prostatectomy, performed in one case by the suprapubic and in the other by the perineal route. It is an entire misconception to suppose that either of these operations, or transurethral prostatic resection, effects complete removal of the prostate. In both types of open operation some of the normal prostatic tissue persists in a compressed state in the form of the surgical capsule, and after all these operations recurrent benign hyperplasia or prostatic carcinoma may develop. Both the author's patients had been kept under observation subsequently and were known to have remained free from symptoms during the intervening period. In 5 similar cases found in the records of the Mayo Clinic the average interval between the prostatectomy and the development of carcinoma was 16 years. In the discussion which followed mention was made of the fact that at the Mayo Clinic at the present time transurethral resection is practised to the virtual exclusion of all other methods of treatment for benign prostatic hypertrophy because the mortality and morbidity are lower, the hospital stay is shorter and the functional result equally good. Since the removal of the prostate by open enucleation is in any case incomplete there is nothing to choose between transurethral resection and open operation as a prophylaxis against recurrence of benign hypertrophy or the development of carcinoma.

Carcinoma: symptoms, signs, and treatment.—During twenty years (1920–40) the death rate from prostatic carcinoma per 100,000 of the male population of the United States of America increased by 62·7 per cent, chiefly because of the increasing longevity of the human race. Kahle and Beacham consider that carcinoma of the prostate will never be diagnosed early enough for treatment to be successful until every male patient over the age of 50 years, whatever his complaint, is rectally examined. Early diagnosis is hindered by the insidious onset of the disease and by the great incidence of associated disease which often causes the prostatic symptoms to be overlooked. Urinary obstruction is often a late symptom and even the pains of metastases may be attributed to rheumatism and to age. The disease therefore is usually advanced when advice is sought. Radical perineal prostatectomy is then impossible and the form of treatment that can be given can have as an aim only the postponement of death and the relief of pain. Multiple malignant disease was present in 15 per cent of 46 necropsies performed among the 88 fatal cases discussed by the authors. The post-mortem examinations showed extraprostatic extension in 13 cases and metastases in 9. Of 47 non-surgical cases 24 patients died within a week of admission to hospital. In 41 surgical cases 22 transurethral resections gave some prolongation of life and comfort to 10 patients. Among recent and more hopeful measures stilboestrol administration is to be preferred to orchidectomy. Castration aims at the elimination of the androgens which stimulate cancerous growth but simultaneously it eliminates a second testicular hormone which controls pituitary activity. The resulting pituitary hyperactivity stimulates extratesticular sources of androgens such as the adrenal cortex. Thus the benefit derived from castration is brief and the effect of supplementary administration of stilboestrol is modified. Adequate estrogen treatment consists in administration of stilboestrol in daily doses of 5 milligrams for 40 days, and thereafter doses of 5 milligrams thrice weekly until the prostate appears to be normal. The preparation should be administered intramuscularly in oil. During the last 4 years 40 patients thus treated have been observed for periods of from a few months to 3 years. General relief in all patients who have survived long enough to receive adequate dosage has been striking. Metastases already existing have regressed and new metastases have not appeared.

Smith and MacLean state that one prostate gland of every 5 removed for benign hypertrophy proves to be malignant and that prostatic carcinoma develops in 5 per cent of all men who attain 60 years of age. For such, castration has lightened remarkably the surgical outlook. Of 15 patients whose cases are reviewed, 7 having metastases in bone, 2 were subjected to castration only. Castration was done after suprapubic enucleation in 6, and in 7 after transurethral resection. One patient died of vesical carcinoma but the remainder experienced rapid relief of pain with concomitant gain in appetite and in weight. In the 2 patients submitted to castration only, obstruction was relieved, and castration was adjuvant to the relief of obstruction in patients who had been earlier subjected to enucleation and transurethral resection. Occasional involution of the primary growth was observed but not the disappearance of metastases that has been reported by other workers; this is perhaps explained by the fact that 8 only of the authors' cases were of over 6 months' standing at the time of the published report. The method of orchidectomy which was practised left the spermatic cord, the epididymis and the evacuated and sutured tunica albuginea in the scrotum, since the patient appreciates and more readily permits a 'partial' castration. Prostatic tissue alone is rich in acid phosphatase. With perforation of the prostatic capsule comes release of acid phosphatase into the blood. An excess of over 6 units per 100 cubic centimetres of serum proved to be a reliable index of metastasis. Some 2 months after castration a lower level should be established the maintenance of which will coincide with clinical success. The post-operative rise in alkaline phosphatase is possibly correlated to osteoblastic healing of skeletal metastases. The authors believe that stilboestrol should be administered when castration has failed to give lasting relief as the oestrogen is antagonistic to the androgens of known maleficence in prostatic cancer. In this series of cases stilboestrol required to be given to only one patient.

Seventy-five patients with prostatic carcinoma who were treated by orchidectomy and were observed for at least 21 months after operation, are reported on by Nesbit and Cummings. All except 4 of the patients had infiltrating growths. They were divided into two groups: group (1) which comprised 32 patients without clinical signs of metastasis at the time of operation, although in some cases X-ray examination or phosphatase determination yielded evidence of bony involvement; group (2), 43 patients, with pain, cachexia or other clinical evidence of advanced cancer. Of the former group 4 died within the period of observation, of the latter group 21. The average duration of life in group (2) was 11·3 months. Group (1) showed 6 failures still living, group (2) showed 10 failures. In group (1) 22 patients, in group (2) 12 patients, were still alive and well. The most spectacular feature in the successful cases was relief of pain. Urinary obstruction was partially or wholly relieved in all cases in which it was present. The authors recommend the delaying of orchidectomy until symptoms of advanced disease arise, as they believe that thus the maximum period of symptomatic relief may be secured. In most cases the objective signs showed some regression after orchidectomy; in 4 they completely disappeared.

Orchidectomy and stilboestrol.—Barringer, of the Department of Urology of the Memorial Hospital, New York, considers that the present position in regard to prostate carcinoma has improved from one of almost hopeless prognosis to one in which some measure of control

seems to be possible in half the number of cases; what the future holds is not known, but the dramatic improvement in some patients after orchidectomy combined with hormone medication is encouraging. Irradiation treatment by radium-bearing needles or radon seeds has afforded control in 21 of 352 cases (6 per cent) for periods of between 5 and 19 years. Irradiation has been of value in maintaining the patency of the urethra and so enabling a patient to empty his bladder. Deep X-ray treatment has been of little use in the control of the disease. Radical removal of the small prostatic carcinoma has also effected a cure in a low percentage of prostatic cancer. Four factors in the pre-orchidectomy period were found to be of great value in the orchidectomy period. They were (1) aspiration biopsy, (2) transurethral resection, (3) the common occurrence of bony metastases, which are generally osteoplastic, and (4) the acid and alkaline serum phosphatase determination. Stilboestrol is recommended to be given in large daily doses orally (5 milligrams) because castration is not a completely successful anti-androgenic procedure. Stilboestrol controls pain, causes recession of the prostatic growth and improves the general condition but rarely has any effect on the bony metastases and therefore should be used only in combination with orchidectomy. The author is of the opinion that orchidectomy and stilboestrol should be the treatment in all cases of prostatic carcinoma and should be preceded by transurethral resection if urinary retention is a dominant factor; transurethral resection is not necessary for diagnosis, aspiration biopsy is sufficient for this. If the prostatic carcinoma is small, confined to the prostate and periprostatic region, irradiation of the prostate or the operation of total prostatectomy should be considered.

Failure of orchidectomy in a series of cases.—Kretschmer reports on 11 cases in which orchidectomy was performed for cancer of the prostate gland and condemns the prevailing idea that such treatment is all that is necessary in order to effect a cure of the disease. The procedure is of recent origin and insufficient time has elapsed to permit an accurate evaluation of results to be made. The results of orchidectomy in the author's group of cases were unsatisfactory and compare unfavourably with similar recorded cases. Three patients died 5, 8 and 11 months respectively after operation. One patient remained confined to bed and required frequent doses of morphine. Three patients continued to suffer pain, and one had pain on micturition and periodic haematuria. One patient stated that he was improved 11 months after orchidectomy, and 2 others also reported improvement after a few months. Some of the patients felt better immediately after the operation but 2 of them died shortly afterwards. Misconceptions concerning the efficacy of castration in the treatment of carcinoma of the prostate gland should therefore be corrected.

Stilboestrol given intramuscularly.—Kahle, Schenken and Burns report on 5 cases of prostatic carcinoma which were treated with stilboestrol or stilboestrol dipropionate. One patient was first seen in September 1940 after symptoms had lasted for 18 months and he was then bedridden. He was receiving only temporary relief of pain by administration of large doses of morphine. The enlarged and nodular prostate was stony hard and metastases involved the femora, pelvis, vertebrae, ribs and probably the lungs. Relief of urgent pain was attained by subarachnoid alcoholic injections. From October 1940 to February 1942, 503 milligrams of stilboestrol were administered intramuscularly with clinical and X-ray improvement after the first month. Pain which returned in March 1941 was alleviated by further subarachnoid alcoholic injections which unfortunately also produced permanent vesical paralysis, constipation and neuritis of the lower limbs. Nevertheless the patient was restored to business life and drove his car. After another year's improvement there was a relapse in August 1942 which was countered by increasing the dose of stilboestrol from 5 milligrams at 5-day intervals to 5 milligrams daily for 40 days; then the dose was reduced to the same amount given on alternate days for 40 doses, and finally to 5 milligrams 3 times a week. This produced minor gynaeccomastia but proved that resistance to stilboestrol does not necessarily develop. After a total of 1,000 milligrams had been given, the prostate in February 1943 appeared to be normal with progressive regression of metastases. The second patient was not cooperative; he received 75 milligrams only of stilboestrol, treatment being wholly rejected for 124 days before his death from causes other than malignancy. Necropsy showed, however, pronounced regression in the prostate, macroscopical and microscopical, and absence of metastases. The three other cases did not show metastases. In addition to displaying equal clinical improvement they afforded opportunity of serial histological examination. The regression in one of these cases attained complete disappearance of carcinomatous cells. Castration, which is often contra-indicated by the patient's condition, does not appear to be a desirable adjuvant.

Stilboestrol given by the mouth.—Fergusson had 18 cases of carcinoma of the prostate under treatment with stilboestrol by the mouth in the course of 15 months. He concludes that this form of therapy is of value in many instances and may render suprapubic drainage unnecessary, although there is always the possibility that co-existent urinary obstruction may require surgical intervention. In each case the diagnosis was established by means of palpation and biopsy of the prostate, measurement of the serum acid phosphatase and X-ray confirmation of the presence of bone metastases. It was found that when 5 milligrams of stilboestrol were given twice or thrice daily and when this amount was reduced relatively to the fall in the level of the serum acid phosphatase, a rapid response was produced in favourable cases. Of the 18 patients, 10 were either moribund with advanced carcinoma or with urinary failure on admission, or died from other causes; 6 of the 8 survivors ultimately became virtually symptom free; the other 2 showed little improvement but their condition did not deteriorate.

The side effects of the treatment were few; the commonest were tender enlargement of the breasts. It was also found that complete discontinuance of the oestrogen was likely to be followed by a return of symptoms, but that a maintenance dose of 1–2 milligrams twice daily often sufficed to prevent recurrence.

Effect of stilboestrol with or without orchidectomy.—Cancer of the prostate gland treated with stilboestrol only, by orchidectomy only or by a combination of the two is discussed by Herger and Sauer. A year's study comprised 82 patients. Sixty who received stilboestrol alone attained the local improvement of shrinking or softening of the tumour in 30 instances but general improvement was manifest in 13 only. These figures include 10 patients having metastases in bone or lymphatic glands of whom 3 manifested general improvement. Orchidectomy alone was employed for 3 patients. Although all had metastatic growths improvement local and general resulted. Stilboestrol and orchidectomy combined were employed for 19 patients of whom 17 had metastasis. Local improvement resulted in 14 of whom 10 manifested general improvement. The relief of pain or obstruction, the diminution or softening of the tumour and, in patients with metastasis, the decline in serum acid phosphatase activity are criteria of favourable response to treatment. Such favourable response followed treatment with stilboestrol alone in 21·7 per cent of cases and by castration alone or combined with stilboestrol in 51 per cent. When the cancerous prostate is still encapsulated surgical removal remains the undisputed procedure. Castration is the palliative treatment most often successful and should be recommended to patients with metastasis or with rapidly growing tumours or to those unresponsive to stilboestrol. When castration fails stilboestrol fails and its value in reinforcing castration is not proven. Patients who decline both operations, patients without distressing symptoms and patients of slow deterioration may advantageously be treated with stilboestrol. X-ray irradiation is inferior to any of these alternatives; the mitigations of transurethral section and suprapubic cystotomy will still be required as occasion arises.

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PRURITUS AND PRURIGO (HEBRA)

See also B.E.M.P., Vol. X, p. 165.

Pruritis

Pruritis ani

Treatment by tattoo-neurotomy.—Cantor divides pruritis ani into two categories, (1) secondary and (2) cryptogenic. The treatment of the former is that of the cause. In cases of the latter type which fail to respond to external applications or to injection of anaesthetics in oil the procedure of tattooing with mercuric sulphide is suggested. This was tried because it was noticed that cutaneous secondary syphilides did not involve any area of skin that had been tattooed red for ornamental purposes. Mercuric sulphide is believed to act by poisoning the sensory end-organs. The tattooing is carried out under local anaesthesia by means of a special electrically driven instrument. Afterwards, subcutaneous neurotomy is performed, that is to say the skin is separated from the subcutaneous tissues by means of artery forceps which are introduced through an incision at each lateral edge of the tattooed area and are brought out through another incision in the middle line. Over 90 per cent of cures are claimed for the procedure.

Cantor, A. J. (1943) *Amer. J. digest. Dis.*, **10**, 254.

PSORIASIS

See also B.E.M.P., Vol. X, p. 187; and Cumulative Supplement, Key No. 1312.

Morbid anatomy

Histopathological changes

Biopsy records of 225 cases.—A study of the histopathological changes in psoriasis is published by Burks and Montgomery. Specimens were removed for biopsy in more than 225 cases and the findings were considered in connexion with the clinical features and the course of the disease. In the early lesions the first changes seemed to occur in the epidermis and consisted of hyperkeratosis and acanthosis. The epidermal changes may have been secondary to transitory dilatation of the blood vessels. No Guarnieri-like bodies were seen, and there was not any evidence to indicate virus infection as a causal factor. In some cases the corneal layer was

composed of alternating layers of nucleated and non-nucleated cells, which suggested that periods of activity and quiescence alternate in the psoriatic process. Normal mitoses were seen in the basal layer and also in the prickle-cell layer. There was moderate intracellular oedema but no increase in lipid deposits. In the early papules melanin pigment was deficient but disturbance of pigmentation did not persist in healed lesions. The skin adjacent to the lesions appeared to be quite normal and not in any case were there any changes suggestive of epitheliomatous degeneration or of lymphoblastoma. Micro-abscesses of Munro seen in the stratum corneum or prickle-cell layer were formed by migrating leucocytes which were undergoing degeneration. Pseudo-inclusion bodies, which consisted of extruded nuclei from the prickle cells together with fragments of leucocytes, were common in early and active lesions and have also been noted in other dermatoses which show acanthosis. In active lesions the above changes were more fully developed, with a greater degree of parakeratosis and larger micro-abscesses. In quiescent lesions there were typical scaling, hyperkeratosis and general resolution; some foci of activity were seen in apparently indolent plaques. Striking changes were seen in lesions after treatment, with great reduction or absence of parakeratosis, oedema and acanthosis; at the edges of the lesions however there was persistent and increased oedema and vascular dilatation. In cases of psoriatic arthritis, exfoliative psoriasis and pustular psoriasis there were more severe and exudative changes. The diagnosis of a psoriatic plaque is not usually difficult if a well developed papule is examined microscopically, but multiple sections may be required in some cases. Localized neurodermatitis and seborrhoeic dermatitis present similar histological changes but all the various characteristic psoriatic processes are not seen in conjunction in other skin diseases.

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PSYCHONEUROSES AND PSYCHOTHERAPY

See also B.E.M.P., Vol. X, p. 232; and Cumulative Supplement, Key Nos. 1315-1317.

Psychoneuroses

Clinical picture and classification

The disease of fear.—Willius emphasizes the importance of fear in its influence upon the individual and upon the course of civilization. The emotion may be produced by genuine or counterfeit causes. Nervous energy, the vital force resident in the human body, is constantly being utilized, but during sleep its dissipation is reduced in order to allow for replenishment for the following day. With the advent of artificial light the hours of sleeping have become less as compared with those of primitive man. Worry further dissipates nervous energy and often creates insomnia. Fatigue as a consequence ensues; it reacts upon efficiency and a vicious cycle is set up. The complaint of chronic fatigue defies objective analysis but relates to a very real condition. Fear may profoundly upset an individual's mental equilibrium and exhaustion of the nervous system brings in its wake a multitude of complaints referable to different parts of the body. The problem of assisting the subjects of chronic fear and nervous exhaustion is a difficult one. History of a detailed nature is important and requires long and patient elucidation; any attempt at haste obstructs a satisfactory result. Physical examination likewise must be thorough, so that the patient may unquestionably accept the negative finding of organic disease. An explanation of the processes at work is also invaluable.

Somatic manifestations.—Douglas-Wilson discusses somatic manifestations of psychoneurosis, indicating methods whereby the condition may be diagnosed. A history of mental disorders in near relatives, of personal predisposition or of actual previous psychiatric illness was recorded in 92 per cent of his 231 specially referred cases in a military hospital. (1) Cardiac symptoms were present in 53 cases; the average age of the patients was 31.1 years. Particular help in diagnosis was obtained by tracing the relation of onset and exacerbation to mental stress and also to physical effort. Dizziness, palpitation and sighing for breath were distinguishing features; the character of the cardiac pain seldom suggested organic heart disease. (2) Headache was complained of in 131 cases. The symptom was aggravated in various patients by worry, exercise, excitement and heat, and the descriptions of the nature of the pain assisted in diagnosis. (3) Cough was the dominant feature in the respiratory symptomatology, involving (after exclusion of asthmatics) 36 cases. The preoccupation in chest disease was attributable usually to family or personal illness of such nature. Pain was present in two-thirds of the number in this series and gross dyspnoea on exertion in all but 2 patients. (4) Abdominal symptoms, found in 25 instances, gave a false indication of their prevalence, such cases being usually referred to a special clinic. (5) Twenty-two patients reported muscle and joint pains. (6) Of the 13 cases with urinary symptoms (all juvenile immature types), 7 reported nocturnal incontinence since infancy. (7) In 29 cases there was no definite localization of symptoms. The patients of Douglas-Wilson's series readily admitted, on direct questioning, to concomitant mental manifestations. When the onset had been recent, rapid insight into the nature of the disorder was gained by the patients. Symptoms often co-existed in more than one system. An admission to fear of organic disease was common. Somatic symptoms, when due to anxiety states, usually conform to recognizable patterns.

Somatic complications.—Hubble and Rogerson describe an unusual case of a patient with a superior working-class background, a man of great drive and ambition, impulsive and

resentful of failure, who suffered great frustration and anxiety. He twice had alopecia areata, the second attack of which progressed despite the partial relief of anxiety. Multiple subcutaneous nodules then developed and he showed diffuse freckling and a few *café au lait* patches on the skin. Ten years later a third period of severe anxiety was accompanied by the development of auricular fibrillation, which yielded to treatment by quinidine. Von Recklinghausen's disease, characterized by neurofibromas and abnormal pigmentation, is now thought to be inherited as a Mendelian dominant. Among the many abnormalities associated with this disease, alopecia areata is not mentioned in the literature, and it has been found by Hubble and Rogerson often to be preceded by emotional stress. The auricular fibrillation was unassociated in this patient with any organic disease and therefore can be reasonably considered to be a cardiac neurosis. It may be said, therefore, that the psychological disorder was the cause of two of the patient's three abnormal physical states.

Importance of psychosomatic disturbances.—Leadingham considers that insufficient attention is paid to psychosomatic disturbances, which may be confused with or may be superimposed upon organic disease. No race, sex or social level is immune. The cerebral cortex represents one portion of an intensely complex reflex arc and is connected with the autonomic centres. The effect of psychical trauma is to produce behaviouristic or somatic manifestations or a combination of both. Somatic manifestations result from a disturbance of the mind which affects reflexly the autonomic centres and so produces clinical syndromes which vary according to the organ or organs of the body affected. The alimentary and circulatory systems are among the most commonly affected and yield symptoms and signs such as tachycardia, extrasystoles, alterations in blood pressure, dysphagia, anorexia, nausea and vomiting, epigastric pain and intestinal dysfunction. Smothering sensations, even frank asthmatic attacks and the hyperventilation syndrome, are referable to the respiratory system. Menstrual disorders and endocrine disturbances may occur. Altered urinary function, sexual imbalance, headache, paraesthesia and hyperaesthesia and impaired mental ability are frequently encountered. The prognosis varies in accordance with the duration and severity of the illness. If the emotional shock is obvious the response to treatment is rapid. The individual's reaction to and the types of devastating personal experiences as well as the hereditary background combine to produce the ultimate clinical picture. The importance of parental guidance is emphasized. A lasting impression may be made by the attitude towards the patient of the physician first to attend him. Incautious approach may fix the fear or conviction of a particular malady in the subject's mind. Cases which are the result of domestic and social difficulties have usually a satisfactory outcome and respond to a sympathetic and understanding attitude, the moral support of the physician being called for and the minimum of therapy in the form of drugs being applied. The patient's difficulty in appreciating the connexion between his psychical stress and his physical discomforts must be overcome. Patience is the keynote of treatment.

Emotional disturbances and gastric motility.—Evidence exists that irritation of the body and emotional disturbances retard the evacuation of the contents of the stomach not by producing pylorospasm but by depressing gastric motility. Quigley, Bavor, Read and Brofman carried out experiments on trained dogs in order to study the effect on the motor activity of the pyloric sphincter of emotional and various noxious bodily stimuli when they were applied to somatic and visceral structures. The motility of the pyloric antrum and of the duodenal bulb was also observed. A group of 9 dogs, which were not anaesthetized while being studied, was used and permanent cannulae to give access to the stomach and to the duodenum were placed in position. The animals were trained to lie in hammocks and to cooperate during experiments. It is generally recognized that mental disturbances such as worry or nervousness affect gastro-intestinal motility and many workers believe that pylorospasm can be similarly caused. The authors however in their experiments found that ordinary emotional factors or stimulation of the surface of the body or of the gastro-intestinal tract invariably failed to produce pylorospasm. In fact, loss of sphincter tone and motility was observed. Inhibition of the antrum and duodenal bulb generally accompanied the pyloric suppression. The decreased antral propulsive peristalsis was responsible for the simultaneous retardation of gastric evacuation. It is emphasized that retarded evacuation occurred in spite of concomitant sphincter relaxation. The antrum, sphincter and bulb tended to behave as a unit; in its action the sphincter was similar, not opposed to, that of the antrum. X-ray film confirmed these findings. The claim that pylorospasm is readily produced by emotional states or by noxious bodily stimuli is not supported by the authors' observations or by critical consideration of the clinical evidence.

Anxiety states in soldiers.—Sinclair reports on 310 psychiatric casualties in an Australian field hospital. A standard method of examination was used throughout. There were 3 degrees of war stress encountered: stress more than average, 9 per cent of patients; average stress, 37 per cent; no stress, 54 per cent. Over a quarter of the number of cases had also some physical illness; only 6 per cent had been wounded. The mental symptoms either developed or were intensified when the wounds began to heal. There were 8 cases of true blast injury. It was found that the nearer to the forward line the cases were treated the better the result. One hundred and sixty cases of anxiety states were examined. According to the author a state of fear of battle stress is often encountered as an early feature in the history of anxiety neurosis of war. The common symptom was increasing exhaustibility. Hysterical features were

associated with many anxiety states and depression or hypochondriasis was also found. The author states that organic therapy can be of use in forward-line hospitals.

Hysteria with homonymous hemianopsia.—Stewart, Randall and Riesenman record the rare condition of hysterical homonymous hemianopsia accompanied by a hysterical hemiplegia and hemianesthesia. They were unable to find an example of hysterical hemianopsia in the literature. The subject was a soldier of 31 years of age in whom there developed sudden numbness and weakness of the left side of the body and loss of sight in the left half of the visual field. Examination revealed weakness of the left arm and leg, partial anaesthesia of the left side, ataxic gait, intention tremor of the left arm and diminished left abdominal reflexes. Testing of the visual fields showed a left homonymous 'macular-sparing' hemianopsia. A diagnosis of functional disturbance was suggested by the absence of appreciable change over a period of 3 months, by the fact that the degree of paralysis was the same in all the muscles of the upper and lower extremities and by the fact that there was not any facial involvement. The institution of psychotherapeutic measures effected a prompt and dramatic response with complete disappearance of the symptoms.

Prognosis

Rehabilitation of neurotic servicemen.—Rehabilitation of neurotic patients requires continuity of treatment and environment. Minski states that patients in the Forces fall into 4 categories. Most numerous is the chronic neurotic class of peace-time; here the members have been injudiciously enlisted. Next comes a class of persons who are mentally unsuited to the duties allotted, for example the skilled mechanic who is posted to an infantry unit. The present practice of drafting recruits according to vocational suitability is bringing down the number in this class. Thirdly there are the men who are physically unfit for parades and for strenuous duties. Of thousands of men returned to duty in repair shops, to clerical work and to similar postings 75 per cent have proved to be satisfactory. The final category comprises men with neuroses which were induced by the stresses of battle. These possess good personality and good family history. With prompt treatment they recover after 6 weeks and usually are returned to their unit. Soldiers who are returned to duty are housed apart from other soldiers. The wearing of battle dress rather than hospital blue has a good effect on morale. Work, with educational and physical training, is encouraged. Patients who are to be invalided out of the Forces are interviewed by representatives of the Ministry of Labour before they proceed to their former occupations or go to learn new trades at Government Training Centres. On tracing 500 such patients 373 were found to be in employment a year later, but war-time shortage of labour has to be taken into consideration and many now at work will be again unemployed when demobilization begins. Maladjustment, monotony and exile exist in industry also. Hostels and recreational clubs are valuable temporary expedients but for post-war rehabilitation of social misfits colonies are required. Reproduction of neurotic stock there would not exceed similar reproduction in the outside world. The influence of heredity is less potent than that of environment; both should be countered by child guidance clinics and by the supervision of such colonies by experienced psychiatrists.

Diagnosis

Hyperventilation.—Stead and Warren maintain that hyperventilation can produce psychoneurotic symptoms. Voluntary forced breathing in normal subjects produces variable manifestations of cerebral alkalosis such as faintness or giddiness, numbness and tingling of face and limbs. Similar symptoms may occur in anxious patients who involuntarily over-breathe. Sometimes the patient notices that breathing is increased and considers this to be a symptom. The effect of voluntary forced breathing should be tried in patients who complain of faintness or giddiness or of breathlessness without demonstrable organic cause. It is useful not only as a diagnostic test but also as a means of demonstrating to the patient the way in which his symptoms originate.

Psychotherapy

Psychotherapeutic methods

Successful treatment of hysteria by psychoanalysis.—West cites a case of conversion hysteria in an insurance clerk aged 30 years. The presenting symptom was an increasing difficulty in drinking which had started 4 or 5 years previously. Up to the age of 11 years the patient had been fearless but during a fight with a schoolfellow in which he received a glancing blow on the lower jaw he suddenly felt he must run away or he would be 'knocked to pulp'. Later, in adult life, unreasonable fear became attached also to car-driving, to cliff-climbing and to other adventures. In the treatment, school associations were taken first. Free association led to the recovery of memories of early fears of asphyxiation, for example when a cushion was held over his face as a child and in an attack of whooping-cough. There had been constant difficulties between his parents and he recollected actual attacks of fury with his father for making his mother cry. After discovering that his cowardice was due to an imaginary inferiority he went on to blame his father for not training him properly in self-defence and he arrived at the stage of despising his father for faults of temper and weakness of character. At this point the patient changed in his contemporary attitudes. He was no longer afraid of physical consequences; he developed a new efficiency at squash rackets and after tracing his fears to his complicated relations with his father he felt that he could swallow as well as hit and that there were few restrictions to the indulgence of his adult desires. A short review of the differences between adult and childhood aims closed the analysis at the fortieth session and the

patient was able to meet his adult requirements through a revaluation of aim and a reliance upon that 'something more than father' which agreed with his religious convictions.

Effect of added convulsion therapy.—Moriarty and Weil favour the use of combined convulsion therapy and psychotherapy in the treatment of neuroses. From a survey of the literature they find that the results of various convulsion treatments of neuroses are almost uniformly encouraging—better even than the results obtained in most major psychoses. However, when shock therapy has been employed the importance of psychotherapy has usually receded into the background. Of a total of 20 patients treated in the New Hampshire State Hospital, when the combined modes of therapy were used the condition was considered by the authors to be in remission in 10, to be much improved or improved in 9 and to show questionable improvement in one. The authors' impression is that the total effect of combined shock treatment and psychotherapy is greater than the sum of its component parts. The period of stay in hospital was shortened as a consequence of the combined treatment, a matter of importance particularly during the war. Shock treatment (the electrical method was employed) prepared the way for psychotherapy by improving the affective tone and thus fostered the cooperation of the patient. The usual procedure of choice was (1) analytical psychotherapy, (2) from 4 to 6 electric shock treatments and (3) re-education.

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PSYCHOPATHIC PERSONALITY

See also B.E.M.P., Vol. X, p. 260.

Aetiology

Use of the electroencephalogram

Abnormal electrical patterns.—Hill emphasizes the physico-chemical abnormalities of constitution which form the background of cerebral function in cases of dysrhythmic aggressive behaviour. These patients are those in whom an abnormal electroencephalogram was found and they form 65 per cent of the predominantly aggressive group of psychopaths. The question whether or not the cerebral dysrhythmia in these cases is of the same hereditary type as Lennox, Gibbs and Gibbs have found in the convulsive epileptics is important; clinical and electroencephalographic evidence suggest that it may be so. It is probable that from the earliest years an abnormal state of electrical pattern exists in the brain of these patients and that when adult life is reached the functional abnormality is located in those basal areas of grey matter which are particularly concerned with the reception of crude sensation and with emotional expression. There may be some autonomy of function in thalamic-hypothalamic circuits. Hill's investigations suggest that the aggressive outburst, when it is not the expression of epileptic discharge itself, may often be a release phenomenon from an acute failure of cortical inhibition. Hughlings Jackson's concept of 'dissolution at the highest level' may be applicable to this process. The readiness with which this dissolution occurs can be measured in terms of electroencephalographic sensitivity to hyperventilation; the sensitivity is increased by such physicochemical factors as hydration and hypoglycaemia. This sensitivity and the abnormal characters in the spontaneous record are of the same order of cerebral dysfunctions as the dysrhythmia which is indicative of the convulsive tendency. 'The differences between the cerebral events in motor seizures and the cerebral events in aggressive outbursts are perhaps best sought in the site of discharge, its time relations and the degree of spread to other areas.' Petrie said that a series of electroencephalograms of higher-grade mental defectives, especially of the unstable type, would be of interest. Williams suggested that an abnormal electroencephalogram indicated an inborn constitutional defect which might find expression as epilepsy or else as a behaviour disorder such as a constitutionally determined psychoneurosis, psychopathy or psychosis, in the subject himself or in his children. Sargant pointed out that many apparently normal members of the population had abnormalities of electroencephalographic function; they needed only certain biochemical and environmental stresses to turn them into criminals and impulsive murderers. Such stresses were more frequent in war-time. Meyer expressed the opinion that electroencephalography would probably be one of the principal methods for localization of the subtle and reversible emo-

tional phenomena in the field of so-called functional psychoses, in which present histological methods were not likely to succeed.

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PSYCHOSES: THERAPEUTIC METHODS

Treatment

Specific

Convulsion therapy and preliminary curarization.—Bennett reviews the position of shock treatment in psychiatry. Paracelsus in the sixteenth century and Oliver in 1781 used camphor for the purpose of producing convulsions as a curative measure. Meduna, having experimented with camphor, introduced metrazol (leptazol). The merits of administration of metrazol and of insulin and of electrical treatment are here compared. Although insulin according to Ross and to Pollock is more effective than is metrazol a survey of the United States Psychiatric Hospitals shows a waning interest in insulin whereas the use of metrazol increases. The increase in the use of electroshock is however far greater. Two hundred and three fatalities have been recorded, insulin having a death rate of 0.6 per cent, metrazol of 0.1 per cent and electroshock of 0.05 per cent. Risk of injury during convulsions formerly constituted a drawback to treatment by metrazol or electroshock. Mechanical restraint, the administration of scopolamine and the use of spinal anaesthesia mitigated the risk but it still remained. Now the difficulty has been solved by the procedure of injecting curare intravenously 2 minutes before the injection of metrazol or the induction of electroshock. One milligram of curare for each 2 pounds of body weight is required. The partial elimination of fear, the diminution in psychomotor excitement after treatment and the fact that no toxins are introduced into the circulation are greater advantages of electroshock than is its curative superiority. Chronic alcoholism and constitutional psychopathic states, schizophrenic and psychoneurotic states and the affective disorders are the conditions here considered. Depression and anxiety associated with alcoholism obtain little relief and schizophrenia benefits only when affective elements predominate, but the favourable results achieved in affective disorders generally, establishes shock treatment as an important advance in psychiatry.

Camphor shock therapy.—Friedman studies the mental attitude towards and resulting from irritative camphor therapy in 70 male mental hospital patients, the majority of whom had been abnormal for over 5 years and whose powers of communicability in speech and writing could have been described as minimal or nil. Their prospects of early improvement were considered by the hospital staff to be negligible. Segregation as a measure preparatory to treatment led to an individual attitude of anxiety and self-defence which yielded when treatment started to an attitude of collective objection and complaint. The camphor injection produced within half-an-hour sensations of impending and terrifying annihilation with corresponding motor and facial expressions of agitation. The symptoms gained in severity until the patient reached a delirious state which was acute during the first day of treatment and gradually subsided as the next treatment day approached. Experiences of rapid alterations in the patient's relation to space accompanied delirium. With its subsidence mute individuals became vocal and expressed desire for immediate protective action. As the treatments succeeded one another verbal expression progressed from incoherence to intelligible speech. The practice of writing, long abandoned, was resumed in letters which showed increasing urgency. Analysis of the letters revealed complaints of bodily discomforts, some hypochondriacal and some aiming at protection from further treatment; some may be distilled down to fear of castration. Simultaneously, actual injuries, even fractures, were disregarded. Sexual trends normal and abnormal reached the surface. Alterations in affect were expressed by sensitiveness to fancied insult and were resented by word or blow, by destructiveness and attempts at self-destruction. It is Friedman's opinion that the psychotherapeutic efforts which should accompany irritative therapy might well avail themselves of such awakenings in the apathetic and stuporous patient.

Prefrontal leucotomy.—Kisker reviews the subject of bilateral prefrontal lobotomy (leucotomy) in the treatment of mental disorders. The operation is concerned primarily with the transection of the neural pathway which connects the thalamus with the frontal association areas. Local anaesthesia may suffice but general anaesthesia becomes necessary in unco-operative patients. Haemorrhage from section of an intracranial artery may result in death within a short time; death may also occur later as a result of blood seepage from lesions of a minor nature. Kisker believes that the factor of prime importance in determining the post-operative picture is the pre-operative personality. In his series of 20 cases he was especially struck by the startling rapidity with which anxiety symptoms and signs of tension fell away from the patient; in so far as intelligence is concerned there was found to be essentially no measurable impairment. Disorientation, emotional reverberations, somnolence and similar conditions intruded and tended to block out the intellectual picture temporarily. Motor automatisms, somnolence, lack of restraint, facetiousness and tactlessness were among the more general behaviour signs which were observed in the post-operative stage. A number of Kisker's cases showed post-operative evidence of euphoria and cheerfulness which bordered on the variety seen in pre-senile dementia. Confusion after operation did not occur so often in

Kisker's series as it did in the reports in the literature; the author does not agree with the contention that lack of such confusion and mental alertness are of bad prognostic omen. With respect to autonomic representation in the cortex the author has noted that leucotomy may lead to vasomotor disturbance, flushing, sweating, lack of sphincter control, generalized restlessness and similar forms of behaviour. Section of the anterior thalamic radiations indicates that neither the personality pattern nor intellectual integration are exclusively a frontal function. The problem of somnolence in connexion with leucotomy requires further elucidation with regard to the sleep-regulating mechanism. In 35 per cent of Kisker's cases marked improvement was observed, not any improvement in an equal number and slight improvement in 15 per cent. Not any however were made worse by the interruption of the thalamo-cortical projections. There cannot be any question of the fact that a large number of critically psychotic patients have been enabled to return to a normal manner of living after bilateral prefrontal leucotomy. Whether the damage to the brain will in later years prove detrimental to the individual is a question which can be answered only in time. In general agreement with others Kisker finds that agitated depressions respond most favourably, but quotes Schrader who had greatest success with schizophrenics.

The results of operation in 6 earlier cases in which prefrontal lobotomy (leucotomy) had been performed by Moersch and his colleagues in the Rochester State Hospital, Minnesota, for various mental disorders left much to be desired, but in these cases the patients had not offered a good prognosis. The authors now report that in 36 additional subjects most beneficial results have been obtained by lobotomy in certain cases of depression; the results were less satisfactory however in cases of schizophrenia. Petersen, working at the same hospital, records that personality studies of human beings who have undergone total or partial lobectomy are informative and that prefrontal lobotomy is almost specific in the treatment of agitated depression. Relief from anxiety is a most striking result but afterwards the patient is generally confused for some days or weeks and untidiness is a disagreeable trait which also lasts for some weeks after the operation. It is considered that the eradication of anxiety is due to severance of the thalamic projection fibres running to the frontal areas of the brain. There are also certain autonomic changes which may be explained better in terms of hypothalamic function. Petersen has studied sugar tolerance and gastric secretion in patients before and after operation and states that further investigations may explain some of the functional changes that occur after prefrontal lobotomy and their relation to the production of peptic ulcer. Love describes various surgical procedures in prefrontal lobotomy and considers that a less drastic operation is preferable to a more extensive method in which all the deep association fibres are cut. The trephine holes should be placed behind the hair-line so that they are not visible when healed. The buttons of bone are replaced so that there is not any depression in the skull. In a series of 42 cases not one patient died and post-operative convulsions occurred in only one.

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PSYCHOSES: SCHIZOPHRENIA

See also B.E.M.P., Vol. X, p. 302; Interim Supplement, No. 17*; and Cumulative Supplement, Key No. 1321.

Clinical picture

Physical and mental development

Part played by the endocrine glands.—From the results of observations made over a period of 16 years upon patients in various mental hospitals, Kerschbaumer concludes that a close correlation can be made out between physical and mental development and that the schizophrenic usually shows evidence of endocrine maldevelopment or insufficiency which forms the basis of a state of emotional immaturity. The author states that he has never yet encountered a schizophrenic patient of perfect physique. Both general and sexual development are retarded. In both sexes the condition tends to be bisexual, the male frequently presenting female physical traits and vice versa. From the underdevelopment of the physical characteristics of sex it is deduced that the psychic sexual characters are also underdeveloped. In cases of manic-depressive psychosis and in the neuroses, congenital developmental defects are seldom noted; in the amentias they are not rare. Schizophrenics on the whole are derived from physically as well as mentally inferior stock, in which the incidence of severe somatic disease is abnormally high. A family history of chronic alcoholism is often obtained. Study of the body build may be helpful in distinguishing schizophrenia from other psychoses and psychoneuroses. The differential diagnosis on psychological grounds alone is often difficult and from the prognostic point of view is of great importance, because the outlook in schizophrenia is much less favourable than in the other conditions for which it may be mistaken. From the preventive aspect the importance of eugenics in the elimination of the faulty stock from which schizophrenics may be produced is emphasized.

Mental symptoms and signs

Acute schizophrenia in a child.—Eickhoff describes a case of acute schizophrenia in a child of

9, the younger of two children of elderly parents, whose family histories both showed schizoid features. The child was severely shocked at birth after instrumental delivery but did not show any symptoms of intracranial damage. She appeared to develop normally, although somewhat slowly and without initiative, until she went to school at the age of 5 years, and was found to be unteachable owing to inability to concentrate. She was regarded as mentally defective and was ultimately sent to a special school. Her history shows, however, a typically schizophrenic lack of persistence of purpose and inability to make renewed efforts. At the age of 8 years, after a fright, the first acute attack developed, in which she became restless, resistive, terror-stricken, faulty in habits and had to be washed and fed; she showed first incoherence and stereotypy of speech and then mutism. A remission followed after 6 weeks, but two acute attacks occurred within a period of a few months, and she was therefore admitted to hospital. An intelligence test showed wide scatter, uneven performance and fluctuation of interest unaffected by encouragement. At first diagnosed as being mentally defective, this child is shown to be psychotic by the acute attacks in which her whole life and personality are changed and she regresses to a lower level, returning again to a higher level during remissions.

Biochemistry

Blood cell and serum content in various substances.—A study carried out by Katzenelbogen and Snyder was designed to determine the content of sodium, potassium, calcium, magnesium, inorganic phosphorus and chloride in the blood cells and serum respectively of schizophrenics. Blood was taken before breakfast from the antecubital vein of 29 schizophrenic patients; this specimen was defibrinated and centrifuged under oil. Any specimen which showed traces of haemolysis was discarded. Judged by the results obtained in a previous control experiment on 12 normal subjects, the values were within the range of normal except in the following instances. (1) In 5 patients the serum potassium was above the maximum figure obtained in the control series. It is pointed out, however, that still higher values for serum potassium have been noted in normal subjects by other investigators. (2) The chloride and the inorganic phosphorus content of the blood cells were above the maximum normal figure in one case each. The authors consider that the variations may have been due to differences in the emotional states of the patients at the time when the specimens of blood were taken, although no signs of unusual emotional disturbance were observed in any patient. Fluctuations in the serum potassium and serum calcium have been reported by the other workers.

Course and prognosis

Factors influencing prognosis

Basing their estimate on a critical study of the literature, Chase and Silverman have endeavoured to forecast the probable outcome in 150 cases of schizophrenia treated with metrazol (leptazol) or insulin, and compare their estimates with the actual results of treatment. They conclude that in cases with a particularly favourable prognosis shock therapy is beneficial in shortening the illness, but is of little value when the prognosis is poor. In doubtful cases it may turn the scale. In the present series of cases, of those treated with metrazol most patients received a course of 12 treatments, but the number varied from 6 to 26. Patients who did well usually showed improvement after 6 convulsions. The patients who received insulin therapy were given an average of 45 treatments, the number varying from 25 to 90. All patients were kept under constant observation subsequently for from 6 to 14 months. The estimated prognosis was good in 43 cases, fair in 33 and poor in 74. The results observed were as follows: of the first group 33 (77 per cent) were classified as improved or much improved; in the second group 15; in the third group only 11. Insulin appeared to give somewhat better results than did metrazol. The chief factors influencing prognosis appear to be the duration of the illness, type of onset, presence of exogenic precipitating factors, presence of atypical and of process symptoms, temperament, and history of a previous attack. The best results are obtained in cases of short duration with absence of process symptoms. Other favourable factors of less importance are atypical symptoms, acute onset, obvious exogenic precipitating causes, previous attacks, catatonic and atypical subtypes, pyknic habitus and extroversion. No prognostic significance could be attached to prepsychotic adjustment, age at onset, sex or family history.

Treatment

Specific

Treatment by anoxia.—Corwin and Horvath describe the effects of anoxia as treatment for schizophrenia in the case of 10 patients who had been in hospital for this disease for periods varying from 3 to 16 years and were now chronically ill. In every patient, except one who had an aortic systolic murmur and anaemia with 60 per cent haemoglobin, neurological and physical examination was negative. The patients inhaled a gaseous mixture containing low percentages of oxygen, 14, 6, 5.2 and 4.2 per cent. In flying, the last figure corresponds to a physiologically corrected altitude of about 31,000 feet. During the inhalations the neurological reactions noted were (1) a stage of restless movements, (2) a myoclonic phase, (3) occasionally slight rhythmic and tonic phases and (4) changes in behaviour. With the lowest (4.2) percentage of oxygen consciousness was lost in from 2½ to 8 minutes; the maximum time of unconsciousness noted was 85 seconds. The time allowed before unconsciousness was terminated depended upon the patient's condition and was never prolonged to the danger

point. There appeared to be no permanent untoward mental or physical effects; no significant mental improvement was noted. The schizophrenic patient shows deviations from the normal in his physiological make-up and it has been suggested that he has a relatively 'rigid' type of physiological response. It is possible that pilots of a somewhat similar 'rigid' type in physiological response might be better fitted for certain types of high altitude flying.

Specific

Prefrontal leucotomy and its restrictions.—Although good results from prefrontal lobotomy (leucotomy) in psychiatric treatment have been recorded, Bennett, Keegan and Wilbur say that results should continue to be investigated and that the operation should be performed only on chronic institutional schizophrenic patients in whom other measures have failed. The radical treatment of lobotomy is not indicated at present except perhaps in cases of chronic disabling obsessive compulsion. The *modus operandi* of the treatment is not yet understood. Beneficial results may follow section of the anterior thalamic radiation from the medial dorsal nucleus of the thalamus to the frontal poles as thereby the link between imagination and emotion may be severed. The place of the brain incision is determined by the insertion of a ventricular needle before the knife blade is entered to pass in front of the anterior horn of the lateral ventricle. A safe depth of insertion in an adult is from 5·5 to 6 centimetres. A small incision is made over a convolution in the arachnoid. The dull blade is passed medially and laterally until the limits of the frontal lobe are approached and is drawn upward from each lateral edge of the incision. The operative risks are not great if the procedure is correct. The mortality of various groups reported to date has been from 1 to 10 per cent. The patient is apathetic and stuporous after operation; he can be gradually trained to dress and to feed himself and to acquire good social habits. He frequently lacks insight and cannot assume responsibility. The family must be instructed to be patient with and to show understanding of childishness or undesirable behaviour for some time after the operation. Some patients are fit to resume employment in from 3 to 6 months. Freeman and Watts say that the progress of a case must be watched for 3 years before the degree of recovery can be assessed.

Convulsive shock therapy

Leptazol shock and spinal injuries.—Easton and Sommers report on the incidence of spinal injuries in 800 mental patients (366 male and 434 female), treated by metrazol (leptazol) shock in 6 Ontario hospitals. In 209 patients (136 males and 73 females) fractures of varying severity occurred in the bodies of one or more dorsal vertebrae, from the second to the eleventh, the greatest number being in the fourth, fifth and sixth vertebrae. Fractures occurred about twice as frequently in males, owing to their greater muscular development, and in both sexes the incidence was higher in ages under 21 years. In a series of 275 cases in two hospitals curare in the form of introcostrin was given intravenously in a dosage of from 10 milligrams to a maximum of 15 milligrams per 20 pounds of body weight, in order to reduce the incidence and the severity of the fractures. A smaller dosage than 10 milligrams does not give sufficient protection to the long bones and the spine and a larger amount than 15 milligrams is apt to cause respiratory paralysis. In 4 cases this complication occurred, but it yielded to artificial respiration and administration of prostigmin. The use of curare in correct dosage reduced the percentage of fractures from 26 to 5·8 and Easton and Sommers consider that it should always be given when metrazol is used. No death in this series occurred from the use of curare, although one is recorded in the literature. The presence of osteoporosis is a strong contra-indication to the use of metrazol without curare, but that of kyphosis, scoliosis, arthritis, nuclear change or old fractures is of minor importance.

Influence of curare.—Bennett discusses the present status of convulsive shock therapy. Metrazol (leptazol) has proved to be of considerable value, but traumatic complications are a serious danger which has caused many workers to abandon the treatment. The author claims that the combined curare-metrazol treatment introduced by him eliminates the risk of traumatic complications. Electrical shock therapy is also safer when preliminary curarization is practised. The curare is given intravenously, the dose being 0·5 milligram per pound of body weight, administered 2 minutes before convulsions are induced. Transient respiratory embarrassment may necessitate artificial respiration and intravenous administration of prostigmin. The best results of convulsive therapy are obtained in cases of affective psychosis, of which only a small percentage fail to improve. In schizophrenia it has proved to be less successful, but is indicated in cases with affective predominance. Treatment should be carried out in an institution at which proper psychiatric nursing is available, not under home or out-patient conditions.

Insulin and electrical convulsion therapy combined.—Ewen has 'followed up' for periods of from 6 to 32 months a series of 100 cases (53 females, 47 males) of schizophrenia in which the patients were treated as in-patients by combined insulin and electrical convulsion therapy. The average age of the patients on admission was 24 years. It has been found that the combined treatment gives encouraging results and that when improvement is obtained it has usually been maintained beyond the period during which strict observation has been carried out. Patients selected for treatment are preferably those with a history of less than a year's illness. Cardiac failure, tuberculosis and renal disease are absolute contra-indications, and restlessness, pyrexia and infective conditions temporary contra-indications, to treatment. The average number of hypoglycaemic treatments given in each case of this series was 65 and of electrical convulsion treatment 25. The average duration of treatment was 3 months.

Traumatic complications included 4 compression fractures of a dorsal vertebra and one fractured mandible. It is desirable to examine the spine by X-rays in every case before and after treatment. Of 100 patients 62 were discharged, 14 were discharged and readmitted and 24 remain in hospital. Of the discharged patients 55 (25 male and 30 female) have remained well during the 'follow-up' period. It appears that severe introversion and negativism are of bad prognostic significance. Patients with the paranoid form of schizophrenia do better than do those with hebephrenia or catatonia. Suitable conditions of life and work after discharge are of great importance in preventing relapse.

Ineffectiveness of electrical shock therapy.—A report on convulsive therapy in melancholia and schizophrenia is submitted by Atkin. The electrical shock method was used for 127 patients. Clinical examination and radiographical examination of the chest and dorsal spine were carried out in every case, and only patients who were free from physical disease were treated. Sessions were held twice weekly. Experience showed that it was not worth while to give more than 12 treatments, since in all cases in which recovery took place improvement was noted after an average of 4.5 fits and the total given averaged 7.5. Two or three fits were induced after recovery appeared to be complete. There was not any occurrence of traumatic complications, probably because old and feeble patients were not treated. All but 10 of the patients were under 55 years of age. The treatment was ineffective in schizophrenia, but appeared to hasten recovery, although not to increase the recovery rate, in melancholia.

Plantar responses in patients given electrical convulsion treatment.—De Wet examined the plantar responses in a group of 25 patients with either schizophrenia or manic-depressive psychosis who were given electrical convulsion therapy. The responses were studied before the fit, immediately afterwards and 1, 2 and 5 minutes after each fit. In all the patients no plantar reflex could be elicited immediately after the fit ceased. A larger number of positive Babinski phenomena were obtained 2 minutes after the fit as against the 1-minute and 5-minute observations; 21 plantar extensor responses occurred in these 75 examinations. The 'withdrawal' response became more noticeable after a fit than it had been before and an exaggerated response in this respect became even more intense 5 minutes afterwards. The author concludes that the absence of a positive Babinski reflex cannot exclude the possibility of epilepsy and that a flexor response cannot be looked on as a negative proof of epilepsy.

Results of shock therapy in the Army.—Stockings analyses a 3-year experience of shock therapy in the treatment of nearly 300 military psychiatric cases. His patients included all types of schizophrenic psychoses and of the mixed schizoid-depressive states, nearly all of recent and acute onset. Convulsive shock was used first and insulin shock if that failed. A complete remission was obtained in approximately 70 per cent of cases and undoubted improvement in 15 per cent. Failure occurred in 15 per cent. Chronic cases were the least responsive. The importance of early diagnosis and treatment is emphasized. Insulin resistance, manifested by inability to produce coma with a dosage of 150 units or over, is a bad prognostic sign. The incidence of major complications was extremely small. In a series of nearly 300 cases treated by convulsive therapy only 2 fractures were encountered. One case of acute cardiovascular syncope occurred which however was responsive to treatment. Of minor complications headache, muscular pains, painful spine and left side cardiac pain are mentioned. No major complication followed insulin therapy; minor effects included delayed after-shock, transient mental confusion and metabolic reactions consisting of pyrexia, profuse sweating, rigor and malaise.

General review of electrical convulsion therapy.—In a study of electrical convulsion therapy, based on a series of 260 cases of mental disorder treated by this method, Henderson, Tod and Daly conclude that the treatment is easily administered, relatively inexpensive and rapid, can readily be given to out-patients and is probably the method of choice for cases of depression. The authors have used 2 types of apparatus, the Solus-Bini and the Ediswan portable machines. Two hours beforehand the patient receives a light breakfast and one hour later a subcutaneous injection of atropine sulphate 1/100 grain to prevent salivation, respiratory embarrassment and vomiting. The bowel and bladder are emptied before treatment. Usually initial settings of 80–100 volts and 0.2 second suffice to produce a major convulsion, but the dose may need to be increased. In general the older and thinner patients appear to require higher doses than the younger and plumper. The seizure may be one of three types, a 'stun' or simple shock, a minor reaction and a major convulsion, which usually resembles an ordinary epileptic fit. Respiration ceases temporarily and it may be necessary to apply artificial respiration. During the post-convulsion phase the patient may become restless and violent, but usually lies fairly quietly and passes into a deep sleep. Panic attacks may occur in the post-convulsion stage but not, as so often happens with leptazol treatment, before the fit; they are not remembered by the patient. Subsequent amnesia may be total or partial. The treatment is given 2 or 3 times in the week. The percentage of recoveries has been highest (64) in the group of involutional melancholia. In other types of depression recoveries total 46 per cent. In schizophrenia, psychoneurosis and paranoid cases the results were less encouraging. Traumatic complications in this series included 4 compression fractures of vertebrae and one fractured femur.

Atkin, I. (1943) *Med. Pr.*, **210**, 302.

Bennett, A. E. (1943) *J. nerv. ment. Dis.*, **98**, 23.

— Keegan, J. J., and Wilbur, C. B. (1943) *J. Amer. Med. Ass.*, **123**, 809.

Chase, L. S., and Silverman, S. (1943) *J. nerv. ment. Dis.*, **98**, 464.

- Corwin, W., and Horvath, S. M. (1944) *J. nerv. ment. Dis.*, **99**, 149.
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 Easton, N. L., and Sommers, J. (1944) *J. nerv. ment. Dis.*, **99**, 256.
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 Katzenbogen, S., and Snyder, E. Rebecca (1943) *Arch. Neurol. Psychiat.*,
Chicago, **50**, 162.
 Kerschbaumer, L. (1943) *J. nerv. ment. Dis.*, **98**, 521.
 Stockings, G. T. (1944) *J. ment. Sci.*, **80**, 550.

PSYCHOSES: PRE-SENILE AND SENILE PSYCHOSES

See also B.E.M.P., Vol. X, p. 342.

Pre-senile psychoses

Pick's disease

Comparison of three cases.—Pick's disease of the brain is a cortical degeneration which is hereditarily transmitted and which affects the frontal, temporal or parietal areas. Malamud and Waggoner describe 3 cases illustrative of the influence of heredity, of the clinical features and of post-mortem appearances. Lowenberg had already described Pick's disease in a patient aged 21 years, the brother of patient (1) aged 25 years, who is mentioned below. From description their mother died of Pick's disease and their grandmother of senile dementia. The early onset which occurred in the case of patient (1) contrasted with the age of onset in patients (2) and (3) who were both over sixty years of age. Patient (1) when first seen was apathetic, confused and defective to psychological tests. A year later he displayed Parkinsonism, incontinence of urine and faeces and helpless passivity. Pyrexia of central origin developed before death which occurred 30 months after the onset of the disease. The disease pursued a similar but slower course in patients (2) and (3) after a life of instability and alcoholic addiction. In their case inheritance was from a grandmother who, herself a victim of Pick's disease, bore 7 children, 5 of whom were similarly afflicted. A daughter, the eldest of the family, before dying of Pick's disease bore 6 children, 3 of whom also had the disease; patient (2) was the eldest of the 3. A son, the seventh of the family, died of Pick's disease after having begotten 8 children, 4 of whom were afflicted. Patient (3) was the seventh child of this family. At necropsy there was in all 3 patients thickening of the leptomeninges, dilatation of the lateral ventricles and atrophy of the corpus callosum. The cerebral hemispheres were asymmetrical in patients (2) and (3). In patient (1) the frontal, temporal and parietal lobes, in patient (2) the frontal lobes only and in patient (3) the frontal and temporal lobes were affected by advanced atrophy. Histological changes severe, moderate and mild are tabulated in accordance with the cyto-architectonic charts of Brodmann. Severe disorganization pervaded the atrophic convolutions. Areas of moderate rarefaction faded into milder abnormalities in areas macroscopically well preserved.

Senile psychoses

Morbid anatomy

Necropsy findings in a man of 107.—Riese and Zfass describe the pathological findings at necropsy of the brain and other organs of a man believed to be 107 years old, who had suffered from dementia for 11 years. There was a minimal degree of cortical (cerebral) atrophy. The cyto-architecture was well preserved and revealed the well known regional variations. The three processes of formation of pyramids, granulation and splindling were obvious. These three types of cortical organization characterize the adult brain. Cellular changes, gliosis, neurofibrillary alterations and senile plaques were all seen, except in the cerebellar cortex. The cellular changes were of only moderate degree and did not lead to complete destruction. The glial reaction was intense. It consisted of neuronophagia, perivascular gliosis, formation of glial symplasms and glial turfs. There was an intense and generalized proliferation of vessels within the white matter of the brain, with disseminated demyelination in the white matter of all cortical areas and in the cerebellum. Processes of repair and regeneration were detectable.

Malamud, N., and Waggoner, R. W. (1943) *Arch. Neurol. Psychiat.*, *Chicago*, **50**, 288.

Riese, W., and Zfass, I. S. (1944) *Arch. Neurol. Psychiat.*, *Chicago*, **51**, 78.

PSYCHOSES: GENERAL

Clinical picture

Psychosis in officers

Effects of war service.—Duval discusses psychosis in officers as it occurs in the present war. Functional mental illness is determined by the degree of adaptational stress and by the degree of vulnerability of the personality. Exhaustion, insecurity, homesickness, and fear of being afraid, all play their part. One hundred officers were studied. A diagnosis of dementia praecox was made in 30 cases, manic-depressive psychosis in 34; there was undiagnosed psychosis in 14 cases, psychoneurosis in 7, paranoid state in 6; 3 were without psychosis; dementia paralytica was found in 2 and the remaining 4 were classified respectively as involu-

tional melancholia, psychosis due to exsanguination, psychosis with psychopathic personality and alcoholic psychosis. Several striking differences were seen in the figures for officers only as compared with total admissions. The incidence of manic-depressives was much greater and of schizophrenia much less. The incidence of paranoid schizophrenia and the paranoid state was also higher among officers. These differences were considered to be due to the higher average age of the officer group. Attention is directed to the absence of anxiety neurosis. The 3 cases without psychosis appeared to belong to the category of psychopathic personality. Seventy-four patients were discharged from hospital; of these 49 had recovered and 20 improved. One death occurred by suicide. The shortest period of military service was one day and the longest 26 years. Five patients were medical men. The ages of the 100 cases ranged from 20 to 49 years. In 27 per cent a history of previous mental disease was obtained. The presence of obvious affective features was characteristic of the entire group. In many cases situational factors were plainly in the foreground. As contrasted with experience in the last war, exhaustion is often minimal. The author compares his findings with those of Baird who stated that he had no hesitation in placing 38.7 per cent of the psychosis in officers of the 1914-18 war in the group of exhaustion cases.

Treatment

Specific

Surgery and the psychoses.—Freeman and Watts evaluate the results of psychosurgery in a series of 204 cases over a period of 7 years. The authors briefly describe the operation of prefrontal leucotomy and point out that affective disorders require minimal interruptions whereas individuals with longstanding obsessive neurosis or schizophrenia require maximal operations. Re-operation was required in 20 per cent of the authors' cases. The two outstanding manifestations of patients for some weeks after the operation are indolence and lack of tact. In many cases the patients are reduced to a state of childishness in the early post-operative stages. Failures may ensue from section of the frontal fibres at the wrong site. A tabular survey of 154 living patients, after an interval of from 6 months to 7 years after operation, shows that 61 per cent were usefully occupied whereas only 12 per cent were necessarily confined to institutions. In a further table 170 subjects who had been operated on are tabulated in terms of their particular psychosis. Involutional depressions (77 cases), schizophrenia, obsessive tension states, psychoneuroses and undifferentiated schizoid states (7 cases) are all represented. Good results were obtained in 65 per cent of the total number of cases, fair in 21 per cent and poor in 12 per cent; the operative mortality was 2 per cent and 7 per cent of patients died after the operation.

Physical treatment

In acute psychiatric states in war.—Sargent discusses the value of physical treatment in acute psychiatric states in war. Convulsion therapy is very valuable in severe depressive psychosis but is ineffective in such conditions as hysteria, obsessional neurosis and schizophrenia unless a depressive or stuporous component has to be removed before other treatment can be effective. Sargent emphasizes that disaster may follow if early schizophrenia is not treated immediately by the induction of insulin coma. Sedation in acute neurosis is often inadequately administered; during the Battle of Britain and the London blitz intravenous injections of barbiturates or paraldehyde by the mouth were found to be best since they acted quickly and might prevent the development of chronic neurosis. Hysterical conversion symptoms should be removed by suggestion while the patient is under the influence of intravenous barbiturate treatment. Loss of weight may be the precipitating factor in individuals with an inherent weakness of personality which has lain dormant for years. A modified insulin therapy has been found to be valuable in a subject of previous good personality who has lost weight and shows anxiety-hysterical symptoms; until he has regained his normal weight he will usually not be nervously stable again. The patient should not be allowed to go into coma and if he should do so must be immediately interrupted by the administration of sugared tea. After 3 hours of mild hypoglycaemia a meal of potatoes should be given; the excessive appetite created causes the patient to consume enough to produce a distinct gain in weight; gains of up to 18 pounds may occur in from 6 to 8 weeks. For chronically hysterical patients such treatment is useless.

Rehabilitation of patient

Psychological methods in minor psychiatric disorders.—According to Skottowe the aim of treatment in psychological medicine should be the restoration of the patient to a useful practical way of living in the community by the most rapid form of therapy available. Cases are to be divided, if possible from the first interview, into those showing (1) predominantly a somatic disease with psychological accompaniments and (2) predominantly a psychological disturbance without somatic accompaniments. A factual explanation to the patient of the illness is of great value. For patients not needing admission to hospital a practical daily life is then prescribed, somatic functions are attended to, sedatives may be prescribed in order to relieve anxiety, depression or insomnia, and short psychiatric interviews are instituted; the social worker supervises the home and social conditions. Such a plan of treatment is effective in some 60 per cent of minor psychiatric disorders. For in-patients, treatment by continuous narcosis is indicated in severe emotional stress and excessive insomnia and exhaustion; it is contra-indicated in acute respiratory infections and in renal disease. Narco-analysis (with dissociation induced by injection of barbiturates) finds its greatest usefulness in relieving

paralytic symptoms and amnesia of hysterical origin. Shock therapy has an especially favourable action in affective disorders of retarded, depressive type, and in stupors and may be produced by insulin hypoglycaemia, by the injection of anaesthetic drugs or by electrically induced convulsions. Prefrontal leucotomy has sometimes been used blindly, but good results have been obtained in relieving the automatically reiterated depressive symptoms of chronic involutional depression and the gross behaviour disorders of chronic psychotic epileptics and paraphrenics. Psychotherapy and occupational therapy have a well recognized place in treatment.

Complications

Pellagra in psychotic patients

Clinical picture.—Hardwick reports 12 cases of pellagra in psychotic patients. Ten occurred among chronically affected patients under treatment. All these patients showed faulty feeding habits such as bolting or surreptitiously disposing of their food. Another possible aetiological factor was dysentery; in 2 patients an attack of Flexner dysentery appeared to precipitate the development of manifest pellagra. The most important factor of all, however, was probably improper dietary. The chief clinical features were the characteristic skin eruption, which occurred in all cases, glossitis, loss of weight, diarrhoea and peripheral neuritis. In the remaining 2 cases psychotic symptoms developing in connexion with pre-existing pellagra necessitated admission to an observation ward. Treatment consisted in the giving of nicotinic acid by mouth or parenterally. The initial dose was 500 milligrams given daily by mouth or 120 milligrams by intramuscular injection. This was subsequently reduced to a maintenance dose of from 100 to 150 milligrams daily by mouth. Eleven patients showed striking physical improvement and one of the 2 admitted for observation completely recovered mentally as well; the other died. The author urges that more attention should be paid to the nutritional state of psychotic patients so that early cases of avitaminosis may be detected and treated.

Duval, A. M. (1944) *War Med.*, **5**, 1.

Freeman, W., and Watts, J. W. (1944) *J. ment. Sci.*, **90**, 532.

Hardwick, S. W. (1943) *Lancet*, **2**, 43.

Sargant, W. (1943) *War Med.*, **4**, 577.

Skottowe, I. (1944) *Lancet*, **1**, 329.

PUERPERIUM

See also B.E.M.P., Vol. X, p. 365; Interim Supplement, No. 10*; and Cumulative Supplement, Key Nos. 1326–1329.

Puerperal sepsis

Treatment

Prevention.—Kenny and Barber describe the system of preventive routine in puerperal sepsis as employed at the British Postgraduate Medical School, London. Patients are divided into 'clean' (those without septic foci and with intact membranes) and 'suspect' (including those with ruptured membranes), and are kept separate. Pyrexial cases go to an isolation block. Dettol (30 per cent cream and 10 per cent lotion) is used for patients and in examinations. The authors report an epidemic of haemolytic streptococcal puerperal sepsis which occurred in spite of these precautions. Diligent search for the source of the epidemic revealed an abundant growth of haemolytic streptococci from the under-rim of the lavatory seat in the receiving room through which all but 2 of the 7 infected cases passed on admission. All the streptococci isolated from the 7 cases proved to be of the same type. After disinfection of this source of infection by means of formalin vapour no further cases occurred. It was considered that probably other articles in the room were contaminated with streptococci and accounted for the origin of the epidemic but since the room was fumigated immediately following the bacteriological findings, definite proof of this theory was lacking. Swabs from the vagina, nose and throat of contact patients and nose and throat of the staff produced some streptococci, but of different types from the infecting agent, as were also swabs from some bed-pans. The number of haemolytic streptococci isolated from the lavatory seat and the fact that they were of the type found in the infected patients provided overwhelming evidence of the real source. Additional precautions in the matter of the application of antiseptics to the external genital tract immediately on admission have now been introduced, as well as a different method of disinfection of the receiving room.

Penicillin successful after failure of sulphonamides.—Mitchell and Kaminester regard as a therapeutic triumph the response to administration of penicillin by a patient with puerperal sepsis the organisms of which had become drug-fast to sulphonamides. In a woman 35 years of age who entered hospital for her seventh delivery, loss of a litre of blood necessitated manual removal of the placenta. After infusion of a litre of 5 per cent dextrose and later of citrated blood the pulse was slow and good. On the second post-partum day the patient experienced a rigor and sulphathiazole was administered orally. Next day general urticaria, indeterminably due to ergotrate (ergometrine maleate), transfusion or sulphathiazole, confused the picture. Sulphathiazole was pretermitted until 5 days later grave symptoms compelled the resumption of sulphonamides orally and intravenously. Improvement resulted except for a mild thrombophlebitis which developed in the left leg on the fourteenth day.

Five days without pyrexia allowed discharge on the nineteenth day *post partum*. On the twenty-first day the patient was readmitted with pelvic thrombophlebitis. Sulphonamides, intermittently administered until leucopenia compelled their administration to be given up, were ineffective, the organisms having apparently become sulphonamide-fast. A haemolytic streptococcus was cultivated daily from the blood from the thirty-first to the fifty-fourth post-partum day, when the patient, despite 9 transfusions, appeared to be moribund. Penicillin, 42,400 Oxford units, was then administered on each of 2 days intravenously. Improvement was dramatic; the temperature fell and blood culture was negative. Decreasing doses, totalling a further 273,700 Oxford units, were administered intramuscularly and subcutaneously during the next 9 days. On the 76th day *post partum*, the patient left hospital completely recovered.

Kenny, Meave, and Barber, Mary (1944) *Brit. med. J.*, **1**, 809.

Mitchell, R. McN., and Kaminester, S. (1944) *Amer. J. Surg. N.S.*, **68**, 136.

PYELITIS

See also B.E.M.P., Vol. X, p. 404; and Cumulative Supplement, Key Nos. 1330–1332.

Clinical picture and course

Acute type

Analysis of one hundred cases.—One hundred cases of acute surgical infection of the kidney are analysed by Duff, Kenyon and Hauser. The fact that one infection may overlap another forbids rigid classification but such infections fall in two predominating groups, namely cases which present evidence of cortical infection and cases of infection complicating calculous or non-calculous obstruction. Severe infection and toxæmia, with extreme tenderness and spasm on the affected side yet relatively minor urographical changes, provide evidence of cortical infection. Such evidence existed in 40 of the authors' patients. Thirty-eight patients had non-calculous obstruction of the upper urinary tract and 42 had impacted calculi. Chemotherapy, which is valuable in early stages, in severe involvement is ineffective and confusing. Some patients had failed to respond to and some were too ill to await the outcome of chemotherapy. Post-instrumental reactions, including 6 after cystoscopic procedures, led to restriction of instrumentation as far as was justifiable and to reliance on excretory urography. Operations performed are listed as nephrectomy 42, decapsulation 18, enucleation of carbuncle 8, incision of cortical abscess 4, nephrotomy 18, pyelotomy 12, pyelolithotomy 12, ureterolithotomy 12, ureterotomy 4, ureteral catheter drainage 28. Ureteral catheter drainage proved to be an inadequate procedure. The maximum preservation of renal tissue although desirable must depend upon the patient's ability to withstand the prolonged and pyrexial convalescence which ensues when a seriously infected kidney is not removed. This is the reason for the common procedure of nephrectomy. When nephrectomy was avoided, decapsulation gave satisfaction in cortical infection, with pyelotomy when required for the relief of obstruction. Drainage by nephrostomy was reserved for kidneys with a cortex attenuated by dilatation. Carbuncles were enucleated when possible; the results were not uniformly satisfactory. The immediate establishment of urinary drainage is an essential in the treatment of obstruction in infective conditions.

Chronic type

General review of secondary pyelitis.—Peel suggests that pyelitis is encountered as a secondary condition much more often than has been supposed hitherto. In many cases acute pyelitis may be a recrudescence of a previous attack or may be in association with chronic latent pyuria. The latter in turn may be secondary to some other more serious condition, for example tuberculosis of the urinary tract, disease of the gastro-intestinal tract, stone, some obstructive lesion or a minor congenital anatomical defect. Chronic mild pyuria is common, and many patients who are symptom free or who have vague general symptoms do not seek medical advice. Mental or physical strain and exposure, however, predispose to exacerbations of acute pyelitis, and it should be remembered that acute attacks may be secondary to other conditions such as those described above. A patient with acute pyelitis should not be considered to be cured until the urine has been sterile for a month after cessation of treatment and after return to work or activity. In the acute febrile stage treatment mainly consists of rest and the giving of fluids and of alkalis; antiseptics should be withheld during the early stage since they may cause renal damage. Nephrectomy may be required if suppuration ensues. Investigations such as cystoscopy or pyelography are contra-indicated while pyrexia and toxæmia are present; the urine should be examined microscopically for casts and organisms and blood urea and renal function tests should be made. In many cases a moderate degree of pyuria persists after the toxæmia has subsided and antiseptics should then be given. The use of sulphonamides has to a certain extent supplanted that of mandelic acid; according to the author, sulphonamides should be reserved for cases in which special indications for their use exist. The infecting organisms and the presence or absence of nephritis are factors which must be considered in the choice of treatment. Sulphonamides are generally contra-indicated when there is renal involvement; a raised blood urea precludes the use of both mandelic acid and the sulphonamide compounds. In any case the possibility of toxic effects from sulphonamides must be borne in mind and patients receiving them must be carefully watched. In cases of chronic pyuria it is essential to make an accurate diagnosis and to carry out a full urological examination whenever necessary. Surgical procedures may be required to

eliminate organic lesions. Cystitis, which often exists concurrently, generally subsides when the pyelitis is treated but in some cases bladder lavage is necessary. When chronic pyuria cannot be treated surgically, treatment similar to that outlined for acute infections should be given; hexamine is sometimes beneficial. The patient's general health must be improved, and undue exposure and physical or mental strain must be avoided.

Duff, J., Kenyon, H. R., and Hauser, J. W. (1943) *J. Urol.*, **50**, 141.

Peel, A. A. F. (1943) *Practitioner*, **151**, 347.

PYLORIC OBSTRUCTION

See also B.E.M.P., Vol. X, p. 426; and Cumulative Supplement, Key Nos. 1334–1336.

Hypertrophic stenosis of the pylorus

Clinical picture

Two cases in adults.—Two cases of simple hypertrophic pyloric stenosis in adults are reported by Berk and Dunlop. The results of blood studies were normal. Wassermann and Kahn tests were negative. The symptoms in both cases resembled gastric ulcer. On a rigidly enforced ulcer regimen the patients became asymptomatic. X-ray examination, however, revealed that the antrum was thickened and could not be distended on forced filling. Malignant infiltration could not be excluded except by the findings at exploration. Gastric resection revealed hypertrophy of the pyloric muscle with signs of chronic gastritis. Recovery was good in both cases. Hypertrophic pyloric stenosis as it occurs in infants is usually not associated with organic disease near the pylorus. The discovery of gastritis or ulcer in adults should exclude the diagnosis of simple pyloric muscle hypertrophy as the primary disease. Although before the operation the mucosa appeared to be normal in the authors' cases chronic gastritis was shown histologically in the resected stomachs. The authors consider that in their cases this was not a significant aetiological factor. The personality of the patient is a factor of great importance in causation. Under psychological conditions which produce mental strain and stress there may be recurrent pylorospasm resulting in a fixed hypertrophy of the pyloric muscle. The authors considered that subtotal gastric resection in both cases was indicated because a pyloric mass, the exact nature of which was uncertain, was revealed at operation. They state that in similar cases, in which the possibility of a malignant growth cannot be excluded, gastric resection is preferable to simple palliative measures.

Berk, J. E., and Dunlop, H. J. (1944) *Ann. Surg.*, **119**, 124.

PYREXIA OF OBSCURE ORIGIN

See also B.E.M.P., Vol. X, p. 440.

Aetiology and diagnosis

Fever in children

Bakwin observes that infants who remain in hospital for a long time often acquire infections, usually of the nose and throat. Febrile episodes commonly occur for which no cause can be found. The author describes 5 such infants with fever which developed after admission to hospital and which persisted for from 3 to 8 months. The first and second infants were in the hospital because the mother had tuberculosis in the one case and syphilis in the other. The third was admitted at 5 weeks of age with ulceration of the cornea. The fourth child was admitted at 13 weeks because the mother had died, and the fifth at 14 weeks of age for mild vomiting and diarrhoea. The interval between admission and onset of persistent fever varied from 7 to 18 weeks. The usual temperature range was 101–103° F. No definite cause for the fever was found. In some instances the pharynx was reddened or an cardrum was inflamed but these conditions were not striking or persistent. Repeated blood cultures were sterile. Cultures from the throat occasionally showed pathogenic bacteria but fever persisted after the organisms had disappeared. Agglutination tests for typhoid, paratyphoid and abortus fevers were negative. The giving of sulphonamide drugs sometimes resulted in a temporary fall in temperature but continued use of the drugs did not help, nor did keeping the infants out of doors. They were pale, apathetic, uninterested in their environment and unresponsive to friendly advances. Their appetites were indifferent. There was prompt, striking and permanent improvement soon after they returned home. In children, rises of temperature have been ascribed to emotional upsets. Psychogenic fever may occur in nervous children whose temperature is taken daily by an over-anxious mother. It is probable that the profound alterations in behaviour in infants which result from prolonged residence in hospital are chiefly due to emotional deprivation. Because of the relative inactivity of a baby in hospital infected material may accumulate in the nasopharynx, but there is no evidence to support this. It is conceivable that the fever which occurs in infants in hospital is actually due to infection and that psychic disturbances lead to an altered reactivity and a prolongation of the course.

Bakwin, H. (1944) *Amer. J. Dis. Child.*, **67**, 176.

RABIES

See also B.E.M.P., Vol. X, p. 446.

Bacteriology, pathogenesis and pathology**Infectivity of patients' saliva**

Data from an American series.—Sulkin and Harford have taken advantage of the opportunity presented by an outbreak of human rabies in St. Louis, Missouri, to investigate the infectivity of the patients' saliva. Thirteen people were bitten by a stray dog which was then shot. Examination of the animal's brain revealed numerous Negri bodies in the *cornu ammonis*. Of the bitten people 11 received local treatment, namely cauterization of the bites with phenol and afterwards Pasteur treatment. One person refused Pasteur treatment and one could not be traced. Of the 12 known victims, 3 died. Of these 2 had received Pasteur treatment and one was the individual who had refused it. The 3 fatal cases occurred respectively in (1) a boy of 7 years of age who received multiple bites about the head and who was given a complete course of 12 injections of Harris vaccine; (2) a man of 33 years of age, bitten about the head and face, who received 11 injections but who failed to return for the twelfth; and a man aged 24 years who had been bitten on the lips who had refused Pasteur treatment. Specimens of saliva were obtained from 2 of these patients, in both of whose brains Negri bodies were demonstrated *post mortem*. Since several viruses have been found to withstand treatment with anaesthetic ether this agent was used to eliminate bacteria from the saliva prior to intracerebral inoculation into mice. In other mice untreated saliva was used. All the inoculated mice were observed for 35 days. One specimen of saliva, obtained during a convulsive seizure, was found to contain active virus. It is suggested that the virus may be present in recognizable amount only in the copious secretion produced during convulsions and that this may account for reported failures to recover it. Attendants should take care to avoid contact with saliva of patients with rabies.

Sulkin, S. E., and Harford, C. G. (1943) *Ann. intern. Med.*, **19**, 256.

RADIOLOGY IN DIAGNOSIS AND TREATMENT

See also B.E.M.P., Vol. X, p. 456; Interim Supplement, No. 20*; and Cumulative Supplement, Key Nos. 1340–1343.

Systematic radio-diagnosis**Alimentary tract**

Priodax in cholecystography.—Apart from a dietary difference before the use of priodax in cholecystography, Bryan and Pedersen concur with the opinions expressed by Hefke on its value in diagnosis. Sodium tetraiodophenolphthalein (iodophthalein) has hitherto given results satisfactory to the radiologist, but to the patient it has the drawback of inducing diarrhoea, nausea and vomiting, and a blander agent should be sought. Priodax (*p*-(4-hydroxy-3 : 5-diiodophenyl)- α -phenylpropionic acid) affords a satisfactory substitute. Bryan and Pedersen suggest that the patient should take, the night before he is to be examined, his customary unrestricted supper and after it 3 grammes of priodax in water. A fat-free breakfast of tea and toast should be taken next morning before the first examination. Usually a synthetic fatty meal of cholex is taken preparatory to re-examination half an hour later. Hefke prefers to give a fat-free supper, then priodax and thereafter water only until examination next morning. A morning enema should be given. The toxicity of priodax is comparatively low. Excretion is mainly by the urine, hence the absence of the undesirable intestinal symptoms which are caused by tetraiodophenolphthalein excretion by the colon; the absence of opaque matter in the colon greatly aids the differentiation of the gall-bladder from the hepatic flexure. Patients who have experience of both preparations prefer priodax. Bryan and Pedersen state that of 845 patients examined one-third of the number experienced mild diarrhoea, one-fifth were slightly nauseated but only 12 vomited. Of the total number 618 showed a gall-bladder wholly normal which emptied 50 per cent after the fatty meal. In 227 cases malfunction was observed, due in half the number to cholelithiasis. In the 69 malfunction cases so far surgically explored the X-ray finding was in every instance confirmed. In one case only operation disclosed stones not detected radiographically. In Hefke's series a similar procedure was followed and the sequelae encountered were even milder. He gave cream for the fatty meal. The degree of emptying of the gall-bladder after the fatty meal is considered significant by him chiefly as regards the presence of non-opaque stones. The administration of pitressin or an enema is recommended if gas obscures the picture. Radiographical findings were again exactly confirmed at operation. In diagnostic accuracy priodax excels tetraiodophenolphthalein.

Circulatory system

Kymography.—Friedman and Friedman report the results of 1,000 cardio-kymograms made during 1940–41. They used a multiple slit kymograph with a grid width of 12 millimetres and a slit width of 0.4 millimetre, a target film distance of 30 inches and an exposure time of 1.5 seconds, employing postero-anterior exposures. Each 12-millimetre grid in the kymograph produces a corresponding 'frame' in the picture, which consists of 12 frames numbered 1–12 from below upwards; each of these represents the same time interval, so that the course of the pulsations can be accurately followed and timed—more easily however on the left side than on the right. Left ventricular, aortic and pulmonary artery pulsations can be plainly visualized, but the pulsations of the left auricular appendage are barely perceptible. On the right border, working from below upwards, the right ventricular contractions are similar in

character to those on the left ventricle, but in the region of the right auricle two types of pulsations appear, one a dominant ventricular wave, the other a low-amplitude auricular impulse. Above this the contours represent the combined efforts of the superior vena cava and of the aorta. If any pulmonary congestion is present it is difficult to determine the character of these right-side appearances. The character, amplitude and time relation of the waves are the indications from which deductions regarding cardiac conditions can be drawn. Functional capacity is indicated by wave amplitude. In the presence of cardiac failure the administration of digitalis produces kymographic changes, which reduce the rate and increase the amplitude of the ventricular waves.

Radiotherapy

X-ray therapy

In cardiac cases.—Leach reports a clinical study on the effect of roentgen therapy on the heart of 85 patients. He dealt with 3 groups of patients. Group (1) consisted of patients with cancer of the head, neck, cervix, uterus or rectum. In this group the chest and the upper part of the abdomen were not irradiated. Patients in group (2) suffered from malignant lymphoma or teratoma. In these the intrathoracic structures as well as other parts of the body were irradiated. In group (3), treatment was given for cancer of the breast, lung, oesophagus or cardiac end of the stomach. The thorax was the region treated and the rest of the body was not irradiated. There is no evidence that the heart was affected by the roentgen irradiation used. A fall of blood pressure was observed during and after X-ray irradiation and although irradiation was a factor, poor nutrition, anaemia, fever and toxæmia were also concerned. A carotid sinus syndrome was noted, but was regarded as due to infection and metastases in the cervical nodes plus treatment. When the thorax is irradiated, an acute radiation pleuro-pneumonitis may develop which may progress to a chronic form with permanent displacement of the heart towards the affected side and partial fixation of the chest wall. Pericarditis developed in 3 patients as a result of radiation pneumonitis plus secondary infection. Otherwise there was not any clinical evidence of organic cardiac disorder. When the thorax is irradiated the vital capacity is almost always reduced. Cardiac arrhythmia as a result of treatment is infrequent. Electrocardiograms were taken before, during and after X-ray irradiation. Minor changes occurred always, but in patients who had the thorax irradiated, there were characteristic modifications in the T waves.

Clinical applications

Grenz ray treatment in skin diseases.—The value of X-rays of very long wave length (Grenz rays) in dermatology is urged by Leitner. They have been used successfully for almost all the skin diseases which respond to X-ray treatment. They have the advantage over ordinary X-rays in that they cause comparatively little damage and can therefore be administered, with due precautions, as often as may be necessary. The penetrating power is low, in accordance with their long wave length; only a minute fraction of the rays reaches the vascular layers of the cutis. Thus nearly the whole of the energy is effective in the skin itself as compared with only about 5 per cent in the case of ordinary X-rays. Contra-indications are acute dermatitis with oedema and exudation, secondary infection with pus formation and a history of previous X-ray treatment. The dose should be so calculated as to avoid strong cutaneous reactions. Telangiectasia or pigmentation may result from overdosage.

Bryan, L., and Pedersen, N. S. (1944) *Radiology*, **42**, 224.

Friedman, L. J., and Friedman, P. S. (1944) *Amer. J. Roentgenol.*, **51**, 29.

Hefke, H. W. (1944) *Radiology*, **42**, 233.

Leach, J. E. (1943) *Arch. intern. Med.*, **72**, 715.

Leitner, Z. A. (1943) *Brit. J. phys. Med. N.S.*, **6**, 114.

RAT-BITE FEVER

See also B.E.M.P., Vol. X, p. 477; and Cumulative Supplement, Key No. 1344.

Clinical picture

Intravenous nearsphenamine

Rat-bite fever is attributed to 2 different infective agents, *Spirillum minus* and *Streptobacillus moniliformis*. The clinical manifestations are similar. In all, 150 cases have been reported in the United States of America, the majority being regarded as *S. minus* infections. Beeson now reports 2 more cases, one in a boy aged 2 years and the other in a woman aged 59 years; both cases were due to *S. minus* infection. The incubation period in the case of the child was 37 days and in the case of the woman 53 days. The fever was of the relapsing type, occurred with intervals between episodes of from 3 to 5 days and reached 104° F. Large irregular erythematous areas were present on face, neck, abdomen and arms. Blood cultures for the streptobacillus were negative in both cases. Mice inoculated with the patients' blood showed the spirillum in their blood on the sixteenth or eighteenth day. Both cases were successfully treated by intravenous injections of nearsphenamine.

Beeson, P. B. (1943) *J. Amer. med. Ass.*, **123**, 332.

RECTUM DISEASES

See also B.E.M.P., Vol. X, p. 502; and Cumulative Supplement, Key Nos. 1346–1356.

Internal haemorrhoids

Treatment

Injection: selection of suitable cases.—The correct selection of cases of haemorrhoids for treatment by injection is discussed by Foote. Failures are generally due to faulty technique or to attempts to cure unsuitable patients. The injection of sclerosing solutions should be used only in cases of uncomplicated internal haemorrhoids of the first and the second degree. Prolapsed piles should not be treated by injection and external haemorrhoids should be excised under local anaesthesia. Other contra-indications to treatment by sclerosing injections are anal fistula, fissure or stricture; pregnancy; severe cardiac, renal or liver disease; malignant growths of the rectum; haemophilia and either spasm or extreme laxity of the external anal sphincter. Injection however is the treatment of choice for patients with diabetes mellitus, pulmonary tuberculosis or severe anaemia and for senile patients. A permanent cure should not be promised because haemorrhoids can recur. The author recommends the use of a 5 per cent solution of pure carbolic acid in almond oil for the initial injection, with a 20 per cent solution in equal parts of glycerin and water for final use. The technique of the procedure is described in detail. By using a proctoscope and after swabbing the part with weak Dettol solution an injection of 3 cubic centimetres of the solution is made at the level of the ano-rectal line, $2\frac{1}{2}$ inches above the pile-bearing area, into 3 areas corresponding to the primary piles. The procedure should be painless, and the mucous membrane should not be blanched. The treatment is repeated within 2 or 3 weeks, the injection then being made in the areas between the piles. The final treatment is given after another interval of 3 weeks; if any of the piles are still soft 5 minims or less of the 20 per cent solution is injected directly into the neck of the pile. The patient need not be confined to bed for treatment. Complications, which may easily be avoided by correct technique, include sloughing, abscess formation, irreducible prolapse, haematuria or minor haemorrhage. In successful cases the results achieved are usually very satisfactory.

Injection and operative technique reviewed.—Whitney and Angelo point out that a haemorrhoid is not a large vein but a redundant pouch of rectal mucous membrane or skin containing a plexus of small varicosities. The authors consider that the frequency of haemorrhoids during pregnancy is dependent upon the secretion of the hormone, relaxin, and its action upon connective tissue. Two types of treatment are discussed, (1) injection and (2) operation. Injection is made high up into the internal haemorrhoidal mass; several injections are often required and may have to be repeated at regular intervals in succeeding years. Two solutions are mentioned, (1) 5 per cent phenol in vegetable oil and (2) 5 per cent quinine and urea hydrochloride, of which (2) is to be preferred. Many cases of prolapsed internal haemorrhoids respond to this form of therapy. The writers apply the following rule to the management of double haemorrhoids. If the external haemorrhoid is reasonably small and soft, injection of the internal haemorrhoid may be tried but if the external haemorrhoid is large and irreducible or if the internal haemorrhoid has also prolapsed, operation is indicated. In a review of 1,056 consecutive cases in rectal clinics, 58 per cent of the patients proved to be the subjects of haemorrhoids, and 26 per cent of the above 58 per cent had double haemorrhoids. Whitney and Angelo employ a posterior sphincterectomy operation and they claim that as post-operative spasm has been abolished intra-anal drains and packs are unnecessary and stricture formation is prevented. An oil anaesthetic (Proctocaine) is employed to enhance the regional and block anaesthesia and to reduce post-operative pain; 1 cubic centimetre is injected into the sphincters on both sides of the anus, into the sphincters and levator and behind the anus and into both buttocks. The main transfixing sutures are placed above the area of sensation. Dilaudid (dihydromorphinone hydrochloride) is preferred for pre-operative narcosis as it is less likely to cause nausea than is morphine. Hot sitz baths are ordered on the second day after operation and the first stool is obtained 48 hours after operation by an oil retention enema followed an hour later by a saline enema.

Carcinoma

Morbid anatomy

Results of operation.—Dukes reports the pathological findings and subsequent progress in more than 1,000 cases of rectal cancer treated by perineal or combined abdomino-perineal excision, and discusses the factors which influence prognosis. For surgical purposes the rectum may be divided into lower third, central ampulla and upper third, the latter including some of the pelvic colon. Cancers with lymphatic metastases situated in the ampulla show less favourable operational results than do those in the upper and lower thirds. Histologically the growths may be divided into 5 grades of malignancy. Extension is both venous and lymphatic; rapidly growing cancers spread through the veins to the liver. The number of lymphatic glands affected varies greatly. Septic absorption from the ulcerating surface stimulates the proliferation of lymphoid tissue; the cancerous tissue exerts little if any stimulus to the production of new lymphatic glands. The greater the number of lymphatic metastases the worse the prognosis; when the glands near the point of ligation of the pedicle are involved the survival rate is poor. About 40 per cent of all patients treated by rectal excision were alive after 5 years, and as of the 60 per cent who died at least 10 per cent died from other causes, surgical treatment may be regarded as curing half the number of cases. Recurrence after 5 years is unlikely, and it is rare for an untreated case to survive for that time. When colostomy

alone was performed the operational mortality was 15·6 per cent; more than half the number of patients died within the year, and none survived for 5 years. The hospital operability rate amongst cases seen at St. Mark's Hospital, London, has risen, with the more general adoption of the combined operation, from 51 per cent in 1930 to 71 per cent in 1936.

Course and prognosis

Prognostic significance of venous invasion.—Seefeld and Bergen base investigations of the spread of rectal carcinoma by lymphatic, perineural and venous channels on 100 specimens removed during 1935 and 1936. The lymphatic route of invasion has received more attention than have the venous and perineural routes although venous invasion has long been recognized and neoplastic invasion of nerves was described in 1842 by Cruveilhier. Cotugno described the perineural spaces in 1770 and later studies in the circulation therein suggest the probability of conveyance by fluid as well as by tissue. In the 100 cases here investigated lymphatic invasion had affected 47. The percentage of glandular involvement was equal in male and female patients. Glandular metastasis affected 63 per cent of patients under 40 years of age and 50 per cent between the ages of 40 and 50; after 60, the percentage fell to 28. Cancer of the upper and middle third of the rectum displayed glandular metastasis in approximately 50 per cent and of the lower third in 40 per cent of cases. Patients to the number of 10 outlived 3 years and 2 outlived 5 years. Perineural invasion affected 30 patients, namely 18 males and 12 females. Glandular invasion was superadded in 20 cases. Age had no bearing on perineural involvement. The 3 divisions of the rectum each accounted for 10 cases. Four patients outlived 2½ years and 2 outlived 5 years. Omitting absent records in both categories, pain was found to be a prominent symptom in 89 per cent as against 50 per cent of patients who did not show neural involvement. Local recurrence was the salient feature; it was found two and a half times as often when there was neural involvement as it was when there was not. Venous invasion affected 20 patients, namely 13 males and 7 females, and was accompanied in 17 instances by glandular and in 12 by perineural involvement. Cancer of the upper third of the rectum accounted for 55 per cent, of the middle third for 15 per cent and of the lower third for 30 per cent of the cases. Four patients survived for over 3 years and one survived for 5 years. Visceral metastasis occurred after venous invasion in the primary growth in 94 per cent of patients, whereas it occurred in only 18·7 per cent of patients in whom venous invasion of the primary growth was not shown. This is a point of great prognostic significance.

Treatment

One-stage abdomino-perineal resection.—Mayo and Twyman report the results of a survey of 90 consecutive cases of one-stage abdomino-perineal resection for carcinoma of the rectum. Each patient was observed for at least 3 years after the operation. Fifty-two of the patients were men and 38 were women; two-thirds of the whole group were between 50 and 70 years of age; the authors state that it is important to recognize physiological age. In 79 cases the operation was performed with the hope of cure; in 11 cases it was merely palliative. It is now realized that even in relatively advanced cases, namely those in which metastases are present, the survival rate for a period of 3 years after operation amounts to 67·7 per cent. Sixty-one patients in the above group survived for 3 years or more: 25 of the remaining 29 patients died from metastases (23 within 3 years); 4 who died from circulatory lesions lived for 3 years or more. The presence of metastases in the regional lymphatic glands was noted to affect the prognosis. The majority of the lesions were of low-grade malignancy: by Broders's method of classification in 17 cases the lesion was grade I, and in 37 cases it was grade II. As was to be expected a greater survival rate occurred among patients with carcinoma of a low grade of malignancy. It is pointed out that in cases of carcinoma of the rectum palpable metastases may exist in the liver although there may not be involvement of lymphatic glands in the excised tissues. Metastasis may occur therefore by way of the blood stream. The authors recommend the use pre-operatively of intraperitoneal vaccine and the routine post-operative administration of oxygen and transfusions of fresh blood in such cases of abdomino-perineal resection, as aids in achieving a low post-operative mortality rate.

Experience confirms the preference of Collier and Ransom for abdomino-perineal resection of rectal carcinoma, performed in one stage. Biopsy, which eliminates non-cancerous conditions, obviates many mutilating operations but adenomatous polypi, although apparently benign, are potentially cancerous and require removal. Three such cases were encountered. Peritoneoscopy, by the disclosure of metastases, often prevents unavailing operation. The authors' analysis concerns 508 patients of whom 285 were cases suitable for radical resection. Of the remainder 37 were inoperable intrinsically, from associated cancer elsewhere or from general conditions. Exploratory laparotomy forbade further operation in 7 patients. Cauterization, radium and deep X-ray therapy were employed for 25 patients in whom the disease was inoperable or who refused operation. Such procedures are purely palliative and should never replace operation when this can and ought to be performed. Emergency caecostomy for obstruction in the cases of 7 patients who were desperately ill failed in 5 cases. Of 144 colostomies, with a mortality of 17·4 per cent, 4 were preparatory to further procedures which were ultimately not undertaken, and 140 were palliative. In the absence of obstruction or severe haemorrhage and tenesmus colostomy proved to be of doubtful value. Of the 285 radical resections, 2 high colostomies, with perineal excision and anastomosis, were considered to be unsatisfactory. Age and infirmity required 9 operations for colostomy and perineal

excision to be done, which involved 2 deaths; in the 5 two-stage abdomino-perineal resections 2 deaths also occurred. The mortality out of 269 abdomino-perineal resections in one stage, according to Miles's technique, was 8.9 per cent, largely from pulmonary complications. The value at operation of spinal anaesthesia is emphasized, and of intravenous infusions; post-operatively broncho-tracheal suction is recommended to prevent pulmonary complications and the use of the Levine tube with suction to prevent ileus. In future the use of heparin may diminish the danger of pulmonary embolism.

Management of the permanent colostomy.—Hutchinson agrees that the discomfort of a colostomy which has been performed simply as a palliative measure in cases of carcinoma of the rectum fully justifies the dread with which patients regard this procedure. Nevertheless he maintains that this discomfort is largely caused, not by the colostomy, but by the lack of control of movements and the blood and pus from the unremoved lesion. Furthermore, the misery which patients without a colostomy endure from partial obstruction, indigestion, diarrhoea, rectal tenesmus and mental discouragement is often insufficiently recognized. Successful after-management of a permanent colostomy can be achieved. It depends first of all upon the performance of an anatomically satisfactory operation and then upon the subsequent control of the faecal discharge by the evacuation of the colon at regular intervals by means of colostomy irrigations, the technique of which the patient should learn thoroughly whilst still in hospital. In addition the diet should be restricted so as to produce a moderate constipation until effective control is gained and then other articles of diet can be added gradually, provided that any particular food which is found to interfere with control is again eliminated. Ultimately the patient will be able to lead a reasonably comfortable and active existence. This makes it all the more important to recognize and treat carcinoma of the rectum in its early stages.

Coller, F. A., and Ransom, H. K. (1944) *Surg. Gynec. Obstet.*, **78**, 304.

Dukes, C. E. (1944) *Proc. R. Soc. Med.*, **37**, 131.

Foot, R. R. (1944) *Med. Pr.*, **211**, 45.

Hutchinson, W. B. (1944) *Northw. Med.*, **Seattle**, **43**, 107.

Mayo, C. W., and Twyman, R. A. (1943) *Proc. Mayo Clin.*, **18**, 438.

Seefeld, P. H., and Bargen, J. A. (1943) *Ann. Surg.*, **118**, 76.

Whitney, E. T., and Angelo, G. (1943) *Amer. J. Surg. N.S.*, **62**, 296.

RELAPSING FEVERS

See also B.E.M.P., Vol. X, p. 584.

Louse relapsing fever or epidemic relapsing fever

Diagnosis and prognosis

Serological considerations.—Three factors make the diagnosis in relapsing fever difficult. First the available methods for diagnosis are inadequate; secondly, the physical signs in the disease vary and are frequently atypical; thirdly, the symptoms to which it gives rise resemble those of other acute intermittently febrile conditions. A multiplicity of strains, the ready evolution of relapse variants and the possible occurrence of antigenic variations complicate the immunological picture of the disease. Stein describes improved methods for making the serological diagnosis more dependable. As a reliable technique for their culture *in vitro* is as yet unavailable, infected blood, despite its known disadvantages, had to serve as the source of the spirochaetes of relapsing fever. When separated from the blood of heavily infected mice and rats by being haemolysed with saponin followed by repeated washing of the spirochaetal suspension with physiological saline, the spirochaetes appeared to have a broad antigenic specificity capable of fixing complement in the presence of serum obtained from man or animals infected with one or other of the recognized strains of relapsing fever, and capable also of producing a macroscopic agglutination of the antigens with serums from the same source. Positive serological reactions were not observed with serums obtained from convalescents from other diseases such as syphilis, malaria, Weil's disease and typhoid or typhus fever. Hyperimmune serums prepared against other pathogens also failed to react. The author considers that the results of these experiments indicate that by this method a relatively stable antigenic preparation is produced—since it remained unchanged after storage in an ice-box for as long as four months—which may prove to be of use in the serological diagnosis of the disease.

Tick relapsing fever or non-epidemic relapsing fever

Treatment

Results of penicillin administration in mice.—The various spirochaetes which cause relapsing fever, and which are endemic throughout the world except possibly in Australia, are probably varieties of the spirochaete discovered in 1868 by Obermeier of Berlin. Equally varied, according to Heilman and Herrell, are their vectors the ornithodoros ticks which infest rats, mice, monkeys, rabbits, dogs and other animals. Fleas and bed-bugs play a doubtful part and fowls do not serve as reservoirs. The onset of fever is abrupt. The temperature rapidly approaches 105° F., persists for from 3 to 5 days and falls by crisis accompanied by profuse sweating; fever recurs irregularly in from 2 to 9 days thereafter. Roseola and herpes with haemorrhages, gastro-intestinal, nasal and conjunctival, are common. Anaemia develops rapidly and

proceeds to renal, cardiac and hepatic degeneration with splenomegaly. Epidemics may carry an 80 per cent mortality. The use of the microscope will eliminate malaria and rat-bite fever. A positive Wassermann reaction may be noted in about 20 per cent of cases. Treatment with arsphenamine—given in adequate doses since the spirochaete readily becomes arsenic-resistant—is confined to the onset, as severe and complicated relapses may succeed delayed administration. *In vitro*, concentrations of penicillin sufficient to inhibit the growth of susceptible bacteria did not inhibit the motility of *Borrelia novyi* used in these experiments. *In vivo*, 54 mice which were heavily inoculated with infected rat blood appeared to be distressed 22 hours after inoculation and tail blood under the oil immersion objective showed more than 25 spirochaetes in each field. Twenty-six of these mice then received subcutaneously 125 Oxford units of sodium penicillin in 0.1 cubic centimetre of physiological saline at 9 a.m., noon, 3 p.m. and 5 p.m., and at 9 p.m. they were given 500 units in sesame oil; the treatment was continued for 4 days. Improvement ensued within 36 hours after administration of penicillin was started and spirochaetes in the tail blood were found to be few or none. During the next 9 days 4 mice showed minor relapse. Only one died, apparently from extraneous causes. The 28 untreated mice deteriorated and 21 died, usually on the fourth day. Blood smears of the 7 survivors showed relapse.

Heilman, F. R., and Herrell, W. E. (1943) *Proc. Mayo Clin.*, **18**, 457.

Stein, G. J. (1944) *J. exp. Med.*, **79**, 115.

RETINA DISEASES

See also B.E.M.P., Vol. X, p. 611; and Cumulative Supplement, Key Nos. 1364–1379.

Vascular diseases

Haemorrhages

Retinal holes without detachment.—Knapp describes 5 cases of peripheral retinal holes without detachment. These cases are to be differentiated from those of macular holes which show a different causation and a different course. The first case was lost sight of. The second and third were observed for 7 and 5 years respectively and no ophthalmoscopic changes were noted; the fourth patient died within 3 months of the original examination, during which time no fundal change occurred; the fifth developed a detachment 6 months after onset. In 3 of the cases the lesion began with a haemorrhage into the vitreous. A point of importance here is that vitreous haemorrhages in older persons are not necessarily due to arteriosclerosis but may result from a retinal tear. From a study of the literature Knapp finds that retinal holes without detachment are unusual. Many believe that an adhesion between the retina and choroid must be present in order to prevent detachment yet the author found no ophthalmoscopic evidence of choroidal change in 3 of his cases. Retinal holes without detachment are considered to owe their origin to cystoid degeneration or atrophy of the retina together with disease in the choroid and changes in the vitreous. Adhesions between the vitreous and retina occur in every healthy eye. Changes in the vitreous, which undergoes liquefaction and contraction, are important in the pathogenesis of retinal detachment. Such a physical change will result in uneven traction at the lines of adhesion with the retina. Movements of the vitreous occur with every movement of the eye-ball and thus exert a pull on the retina. Knapp offers the explanation of non-development of the detachment on the grounds that, whereas retinal changes can explain the retinal hole, the vitreous has not undergone pathological changes of an extent sufficient to cause detachment. Patients with retinal holes must be carefully watched for the possibility of subsequent development of detachment but operative procedures are not indicated on holes in the retina in the absence of detachment.

Retinitis pigmentosa

Associated conditions

Nerve deafness.—Of 12 patients with retinitis pigmentosa presented in a study by Sirles and Slaughter 6 were the subjects of nerve deafness. No other extra-ocular pathological phenomenon so frequently accompanies retinitis pigmentosa and the high ratio suggests more than coincidence. Possibly the morphological kinship of the retina and of the inner ear illuminates the problem. Waldeyer considered the cochlear duct and the choroid coat to be comparable and likened the pigment cells of the ear to those of the eye. The retina develops from the neuro-ectoderm of the forebrain and the organ of Corti, the ampullary crest and the maculae of utricle and saccule develop from the neuro-ectoderm of the hind-brain. Individuals suffering from retinitis pigmentosa often appear to be unaware of hearing deficiency until a large range of hearing has been lost. Four patients were aware of impaired hearing, one of them only because she could hear a knock at the door but not a ring of the bell. Two of the patients were unaware of deficiency in hearing. Audiometric reading is therefore a requisite of accurate testing. Of the 4 patients who were aware of deafness, 3 reported that it was noticeable long before the eye symptoms developed. A reliable report from the fourth was unobtainable. Eugenic studies have indicated the presence of a germ plasm defect in retinitis pigmentosa. Analogy would account for simultaneous deficiency in the organ of Corti.

Tumours

Glioma retinae

Incidence.—Griffith and Sorsby record that 59 children who suffered from retinoblastoma

(glioma retinae) attended the Royal Eye Hospital, London, during the last 50 years. This represents approximately an incidence of one case in 32,790 births in South London. In 53 patients occurrence was sporadic and in 8 only was the affection bilateral. In the 6 consanguineous cases, drawn from 3 generations of a single family, the affection was in 5 cases bilateral and in 4 cases occurred before the seventh month. The literature confirms the theory that genetic origin favours bilateralism and early onset. Genetically, retinoblastoma displays 4 characteristics. (1) The first is sporadic occurrence. In support of the sporadic character of the occurrences in this series, 452 cases from other sources are cited, in which consanguinity of the parents is recorded 3 times only. (2) In the familial manifestation brothers and sisters may be affected although, so far as is known, they do not possess affected antecedents or affected offspring. (3) In the third type transmission from father or mother is direct to child. In the family described a father of untainted antecedents was bilaterally affected. His left eye was excised at the age of 27 months and the right eye spontaneously recovered. He had 5 sons of whom the first died immediately, the third and fifth succumbed to bilateral affection and the fourth, who was unilaterally affected, survived excision and had reached the age of 23 years. The second son, whose bilateral lesion underwent spontaneous cure, had a son who died in early infancy and a daughter who was bilaterally affected. The records of 17 complete sibships which are comparable to this family are available. An incidence of 61 per cent in the total of children in the 19 complete sibships studied suggests dominant inheritance. (4) In this type one parent, personally unaffected but with affected relatives, transmits to the offspring. The dominant inheritance is therefore irregular. Gliomas show wide histological variations. Possibly, gliomas of proved genetic origin may be shown eventually to differ histologically from those which occur sporadically.

Griffith, A. D., and Sorsby, A. (1944) *Brit. J. Ophthalm.*, **28**, 279.

Knapp, A. (1943) *Arch. Ophthalm.*, N.Y., **30**, 585.

Sirles, W. A., and Slaughter, H. (1943) *Amer. J. Ophthalm.*, **26**, 961.

RHEUMATIC INFECTION, ACUTE

See also B.E.M.P., Vol. X, p. 639; Interim Supplement, No. 14*; and Cumulative Supplement, Key No. 1380.

Aetiology

Decrease in incidence and severity

Reasons for improved statistics.—Glover discusses the decline in acute rheumatic infection which has been perceptible for many years and has become greatly accelerated since the beginning of the war. Both incidence and severity appear to have decreased. The mean death rate of acute rheumatism for the 40 years ending 1892 was about 87 per million, or 7 times the mortality for 1942. In 1852, 11·2 per cent of all admissions to London hospitals were for rheumatic fever. For the 5-year period ending 1914 the percentage of medical admissions for rheumatic fever at St. Bartholomew's hospital was 5 and at Guy's hospital 5·4. In 1913 the mortality rate per million was 48. In 1939 it was 23, in 1940 20·5, in 1941 15·4, in 1942 12·1. Rheumatic heart disease has shown a similar decline. The deaths from heart disease in patients under 15 years of age have fallen sharply since 1934. The percentage of London elementary school children found by school doctors to be suffering from cardiac disease was 2 in 1926; since then it has fallen steadily until in 1938 it was 0·68. Chorea also appears to have become noticeably less common. Preventive measures such as the provision of special centres, hospitals and homes for rheumatic children are too recent to have contributed appreciably to this apparent decline in the incidence and severity of acute rheumatic infection. Probably various factors are at work, including the decrease of poverty brought about by the war, the greatly increased provision of milk for all children and of midday meals for schoolchildren, and the decreased urbanization resulting from evacuation. Of these three factors the first appears to be the most important. The main cause, however, seems to be a change in the relation between man and the *Streptococcus pyogenes*. Man appears to have become more immune or the organism to have become less virulent.

Class incidence

Is rheumatism an anaphylactic manifestation?—Levinthal contends that rheumatism is an anaphylactic disease. It originates in the mesoderm and its lesions conform to a morphological pattern. Those lesions, apparently local, are manifestations of systemic disease. Neither metabolic derangement, specific organism nor virus has been proved guilty of its causation, but the relation of infection to rheumatism and the occurrence of rheumatism during many infective diseases remain evident. Weintraud, regarding the disease as due to the specific reaction of the tissues to any protein that has specifically sensitized the cells, quoted Friedberger who by intra-articular injection of horse serum produced arthritis in specifically sensitized rabbits. The proteins or antigens here concerned are dissolved microbial products arising from sites of chronic infection. In gout probably an exogenous antigen is absorbed through a breach of the intestinal epithelium. The phenomena of anaphylaxis are recapitulated and individuals are grouped according to these phenomena. Group (1) comprises individuals so incapable of producing antibodies that resistance to antigens is absent. They succumb to sepsis. In group (2), which includes rheumatic sufferers, the output of antibodies although not wholly lacking is insufficient to prevent some antigen from reaching the antibody in the

reticulo-endothelial cells. Group (3) possesses immunity because of adequate antibody output. Variations in health can transfer individuals from one group to another. The local character of rheumatic lesions is determined by adjuvant irritants such as occupational strains of joints or a cold draught on a neck muscle. The Auer phenomenon illustrates this. An explanation is offered of the contrast between acute rheumatic fever, usually juvenile, and rheumatoid arthritis, usually occurring in adult life. First contact of tissue with an antigen raises antibody from zero to increasing distribution. In rheumatic fever the antigens attack at that critical moment when antibodies are wholly intracellular and the serum void of antibodies. The adult, having long lived in balanced symbiosis with many organisms, is not destitute of circulating antibodies although parity of antibody and antigen has been destroyed by chance enfeeblement. Finally the isolation of streptococci after necropsy is admitted but when the struggle of the rheumatic patient ends in septicæmic breakdown he is no longer a representative of the disease, rheumatism.

Cardiac lesions

Is carditis the result of anaphylaxis?—Rich and Gregory produce experimental evidence to show that lesions which have the basic characteristics of rheumatic carditis can result from anaphylactic hypersensitivity. The view that the lesions of rheumatic fever are the result of a hypersensitive reaction to bacterial products has frequently been suggested but against such a theory was the apparent specificity of the Aschoff body. In the authors' experimental procedure rabbits were sensitized to sterile horse serum under conditions which produce serum sickness, and were killed at periods of 1 and 5 weeks after the systemic reaction had taken place. Examination of the hearts of the animals revealed focal lesions which were in many respects strikingly similar to those of rheumatic carditis. Focal oedema of the connective tissue with swelling and degeneration of the collagen fibrils, inflammatory pericardial, valvular and mural endocardial infiltrations, and cell accumulations containing the peculiar types of cells familiar in the Aschoff body, were all seen. Rich and Gregory have previously demonstrated that generalized vascular lesions identical with those of periarteritis nodosa can result from reactions of the serum sickness type, and further drew attention to the similarity between the arterial lesions of rheumatic fever and of periarteritis nodosa. A marked individual predisposition governing the site at which anaphylactic reactions occur may account for the variation in the features of these two conditions. Skin lesions of the anaphylactic type, for example urticaria and erythemas, are encountered not infrequently in rheumatic fever. Purpura may also be a feature in the latter disorder and in anaphylactic hypersensitivity. Eosinophilia as a local tissue response is common to both conditions. Fever and arthritis are also found in the two diseases. Although serum sickness rarely if ever is productive of permanent cardiac functional damage, Rich and Gregory point out that cases have been recorded in which cardiac disturbances have been present during its course. Microscopical examination of synovial fluids aspirated from affected joints in serum sickness and in rheumatic fever shows identical features. Transient pareses are seen in chorea and during serum sickness, and occasional cases of chorea in the latter have been described. The effect of salicylate therapy on serum sickness arthralgia does not appear to be agreed upon by the various observers. The authors conclude that experimental observations coupled with the various clinical considerations outlined above are at least highly suggestive that the cardiac lesions of rheumatic fever may be the result of hypersensitive reactions of the anaphylactic type.

Clinical picture

Effect of rheumatic toxin on the thyroid gland

The basal metabolic rate.—The possible effect of rheumatic toxin upon the thyroid gland has been investigated by Brown and Wasson, who have performed 154 basal metabolism tests upon 97 rheumatic children of both sexes. Seasonal variations soon became apparent and the readings were therefore placed in three groups according to the season at which they were made, namely July to December inclusive, January to March inclusive, April to June inclusive. Of the 97 children 45 showed a basal metabolic rate below -10 per cent on at least one occasion, and 9 a metabolic rate of below -20 per cent. Readings above the normal were obtained in only 2 children. The average basal metabolic rate was -7.6 per cent, or of all readings -8.7 per cent. Twenty-one children showed lower metabolic rates in the period January to June than in the remaining half of the year; 7 showed an opposite tendency; in 5 the readings were variable. The authors suggest that the low rates in rheumatic children result from the effect upon the thyroid gland of continued infection, and that exacerbation of this infection during winter and spring accounts for the further fall during this period of the year. They believe the source of infection to be chronic sinusitis, which was found in all the children. Cervical adenitis was present in 88 per cent. The skin and hair of many tended to become dry in the winter and spring; this may be related to diminution of thyroid function.

Course and prognosis

Importance of cardiac lesions

In a paper read before the Regina, Saskatchewan, District Medical Society, Murnaghan spoke of the outlook in rheumatic fever. The prognosis in acute rheumatism mainly depends upon whether or not the heart is affected. Of 328 children discharged from the House of the Good Samaritan in Boston—a hospital devoted solely to the study and care of rheumatic fever and its cardiac complications, without clinical evidence of heart disease—77 per cent were still free from signs of cardiac involvement 10 years later; in 22 per cent clinical heart

disease had developed, half of them with, the others without, a recurrent attack of acute rheumatism. Five children had died from unrelated causes. During the same period 672 patients were discharged from the hospital with clinical heart disease. Ten years later 34 per cent were dead, 28 per cent were unchanged, 18 per cent had progressively deteriorated. Treatment includes care during the active period and the prevention of recurrences. Prolonged rest in bed is the basis of treatment in the acute attack. A liberal diet rich in vitamins is given. Rest should be continued until all clinical signs of active infection have subsided and the blood sedimentation rate is normal. Salicylates are of symptomatic value but neither they nor any other drugs, including sulphonamides, have a specific curative effect, although the latter appear to be of some value in prophylaxis. Antitoxic serum is ineffective. Immunization with polyvalent vaccine appears to reduce the number of recurrences. Home teaching and occupational therapy are beneficial once the acute stage is past. The patient is kept under supervision for at least 5 years. He is re-examined at regular intervals and exercise and games are undertaken only as prescribed by the doctor. Tonsillectomy, if thought to be advisable, is performed during a quiescent period.

• **Diagnosis**

In children

Important preventive measures.—Keith recounts his observations on the diagnosis and treatment of rheumatic heart disease, a disease which causes more deaths in persons under 20 years of age than do diphtheria, scarlet fever, whooping-cough, measles, meningococcal meningitis and acute poliomyelitis taken together. The first essential in diagnosis is differentiation between rheumatic and non-rheumatic pains. The former generally occur in children between 5 and 10 years of age and affect the knees or ankle joints. They are felt when the child rises in the morning or in the late afternoon and they disappear when he is warm in bed. If the blood sedimentation rate is raised and joint pains are felt, acute rheumatic infection is probably present. Salicylates usually relieve rheumatic pains whereas the non-rheumatic type is often cured by vitamin B complex. An aortic or mitral diastolic murmur in a child is almost invariably diagnostic of rheumatic fever. The characteristic initial systolic murmur is soft and blowing early in the disease and later becomes harsh. It may be accompanied by an obscured first sound. Treatment, especially of recurrent attacks of acute rheumatism, should be mainly preventive. The danger period is during the 5 years after the first signs of rheumatic infection appear. The 4 most important preventive measures are (1) an optimum diet, (2) diminution of foci of infection, (3) adequate rest and (4) any necessary restriction of exercise, especially after attacks of cold or sore throat. The effects of sulphanilamide in the prevention of recurrent rheumatism are being investigated. Treatment of an acute attack includes rest in bed for a period of 4 months or more, together with administration of salicylates to relieve joint swellings and to reduce the temperature and of digitalis in chronic cases in which heart failure with oedema occurs. Digitalis should be avoided when the liver is enlarged and when oedema is slight, as this drug may give rise to toxic signs.

Treatment

Preventive

Use of haemolytic streptococcal toxin.—Wasson and Brown immunized 101 rheumatic cardiac children with crude N.Y. 5 strain haemolytic streptococcal toxin. The disadvantages of severe local reaction and the necessity for making 19 attendances during each of 2 years caused resort to a tannic acid precipitated toxin of N.Y. 5 strain, whereby reaction was minimized and attendances were reduced to 8 in 2 years. This attenuated toxin was injected intradermally on 4 occasions, 3 weeks apart, in doses of $\frac{1}{10}$ of a cubic centimetre containing respectively 5,000, 8,000, 10,000 and 12,000 skin test doses. The largest dose was repeated half-yearly, beginning 6 months after the fourth inoculation. Forty-two children, average age 10.9 years, including 13 with serious cardiac conditions, constituted the first group. Thirty-three children, averaging 12.1 years, including 5 with serious cardiac conditions, served as controls. In 9 months the patients gained a mean weight of 7.5 pounds and the controls gained 7.9 pounds. Patients reported 1.5 colds per head and controls 2.9. In patients subacute rheumatic symptoms were slight, in controls many and severe. In patients there was not a case of rheumatic fever, among controls there were 11 attacks and 3 deaths. One choreic patient and one with congenital and rheumatic heart disease, chronically uncompensated, failed to improve. Circumstances prevented 11 patients from continuing their attendances. Of 31 reporting after 12 months 29 received their half-yearly injections during the second year. This year 29 children averaging 12 years of age were controls. In patients subacute rheumatic symptoms further abated. Their mean gain in weight surpassed the gain made by the controls. Patients suffered 2 attacks, and controls 6 attacks of rheumatic fever. These results encouraged the authors to treat 38 additional children of an average age of 9.9 years. Again those treated surpassed the control group of 29 in general condition, and in particular one doubtful attack of rheumatic fever contrasted favourably with 6 attacks among controls.

Remedial

Importance of early diagnosis.—Horder discusses the social and economic problem of rheumatic disease. There are at least a million or more sufferers from rheumatism in Great Britain but if all cases of rheumatic disease were diagnosed in the early stages and were promptly submitted to efficacious treatment there would be a rapid and great reduction in

disablement due to rheumatism. Under the stress of war-time conditions there is an even greater need for the provision of effective treatment since war has aggravated the incidence of rheumatic diseases. At present probably not more than 10 per cent of all sufferers from rheumatism in its early stages obtain the treatment required for the arrest of its progress. It is urged that team work among practitioners, hospitals and treatment centres is important for the proper assessment of the various causal factors, namely traumatic, infective, metabolic, nutritional, endocrinal, psychological and environmental. The giving of adequate treatment is outside the scope of one practitioner's capacity and commonly the patient becomes seriously invalided before he can be classed as a suitable candidate for hospital treatment. In such centres as do exist the present methods of alleviation and cure give good results but many more specialized treatment centres are required. A scheme is outlined for establishing these on a regional basis. The plan closely resembles that framed by the Empire Rheumatism Council. To each specialized centre would be assigned the advising and supervising of local treatment centres within the area. Thus would be built up on a national basis a special health service which would make readily available to all sufferers the present valuable but scattered facilities for the treatment of rheumatic diseases.

Intravenous drip method of sodium salicylate administration.—Coburn states that the factor of infection which is an essential component of the rheumatic reaction is not modified by salicylate therapy. So long as this factor is active the rheumatic patient is subject to inflammatory reactions in vascular tissues throughout the body, particularly in the heart. These reactions continue so long as the respiratory pathogen, haemolytic streptococcus Group A, liberates antigen and induces an abnormal antibody response in the rheumatic subject. The inflammatory reaction however can be suppressed to an extent dependent upon the concentration of salicylate in the circulating plasma. The greater the concentration of circulating antibody globulin the higher the plasma salicylate level required. Salicylate concentrations between 100 and 200 gamma per cubic centimetre of plasma may relieve all symptoms without suppressing rheumatic inflammation. Plasma levels of 600 gamma may be required to break an intense reaction at the height of the attack and maintenance levels of about 370 gamma seem to be adequate for continued suppression of the rheumatic reaction. The relation between plasma salicylate concentration, blood sedimentation rate and clinical features was studied. Coburn considers that if the sedimentation rate ceases to rise after 72 hours of treatment and then falls progressively to reach normal values within 14 days, the rheumatic reaction has probably been suppressed and further cardiac damage will be inhibited. On this basis the following schedule is suggested. On the first day 10 grammes of sodium salicylate in 1,000 cubic centimetres of 0.9 per cent sodium chloride are given by the intravenous drip method in from 4 to 6 hours. On the second day, if the patient has any rheumatic symptoms or fever, 20 grammes are given. On the third day the 20 grammes can be repeated, but if the patient is symptom free 10 grammes suffice. On from the fourth to sixth days salicylate infusions are given daily until the sedimentation rate has fallen appreciably. On from the seventh to thirteenth days doses of 1.6 grammes of sodium salicylate with 0.6 gramme of sodium bicarbonate are given orally every 4 hours day and night. After 2 weeks or more in which sedimentation rates remain normal, the patient is allowed a trial week of rest in bed without salicylates. If all goes well he is allowed to be up for increasingly longer periods. If frank symptoms, fever or a noticeably raised sedimentation rate occur, another 2 weeks of salicylate therapy is indicated. Plasma salicylic acid determinations will show the occasional patient who excretes the drug rapidly, conjugates it abnormally, or fails to absorb it properly. All of 38 patients so treated were free from valvular heart disease but in 21 of 63 similar cases in which small doses of salicylate were given, signs of heart disease developed.

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RICKETS

See also B.E.M.P., Vol. X, p. 661; and Cumulative Supplement, Key Nos. 1383 and 1384.

Rickets

Pathogenesis and morbid anatomy

Three degrees of severity.—In 230 necropsies of children under 14 years of age evidence of rickets was found in 107 (46 per cent) by Follis, Jackson, Eliot and Park. Histological appearances at the costo-chondral junctions provided the evidence, radiography except in 6 cases having proved to be deceptive. Slight defects in calcification, vascular invasion of cartilage for short distances only and osteoid borders somewhat exceeding normal are denominated by the authors slight rickets; 53 subjects were affected. Severe defects in calcification, osteoid

borders exaggeratedly wide and extensive, and vascular invasion of cartilage are denominated severe rickets and involved 11 patients. Moderate rickets, an intermediate form, affected 43 subjects. Incidence in white and in negro children differed little but moderate and advanced rickets together showed a percentage of 18 in white contrasted with 27 in negro children, to whom advanced rickets was entirely confined. Age incidence was found to be greatest during the third year and of 67 such necropsies 38 subjects (57 per cent) were affected. Thereafter an incidence of 40 per cent stands fairly constant up to the fourteenth birthday. Rickets does not appear to be specifically cognate to any disease except possibly to lead poisoning, which was concomitant 14 times. Illness may encourage or inhibit the development of rickets. Children who succumbed to disease in less than 14 days showed a 67 per cent incidence of rickets whereas those who died of chronic disease showed an incidence of 41 per cent only. The disparity is inexplicable. Rickets was found to be most prevalent from December to February. Widespread disturbance in calcium-phosphorus metabolism is demonstrated. Administration of vitamin D may be prolonged advantageously up to the fourteenth year.

Follis, R. H., Jun., Jackson, Deborah, Eliot, Martha M., and Park, E. A.
(1943) *Amer. J. Dis. Child.*, **66**, 1.

SCIATICA

See also B.E.M.P., Vol. XI, p. 26; and Cumulative Supplement, Key No. 1389.

Treatment

Subacute and chronic forms

Importance of rest.—In a paper on the treatment of sciatica, which is defined as pain in the distribution of the sciatic nerve, Hurst describes the many divergent views concerning its aetiology and treatment which have been held by different authorities during the past 50 years. First considered to be a neuritis or radiculitis and treated by various injections given into or over the nerve, sciatica came to be held to be due to spinal arthritis, to pressure caused by a prolapsed intervertebral disk, or to fibrositis, and a great variety of treatments were advocated. In this great diversity of symptoms and treatment Hurst finds a large element of unconscious suggestion and hysteria. He considers the rational treatment of sciatica to be complete rest in bed from the onset, with perhaps, in exceptionally severe cases, fixation by means of a plaster spica. Rest in bed should be combined with simple psychotherapy designed to promote expectation of rapid recovery and rapid rehabilitation, and thus to prevent the development of hysterical continuation of pain and disability. Even when hysterical sciatica has become established it may be cured by simple psychotherapy in the form of explanation, persuasion and re-education. Some few patients who do not get well after a month of complete rest in bed may give a history and show signs of root pressure, probably due to trauma. The removal by operation of the herniated intervertebral disk effects a cure. After operation the same encouragement should be given to the patient to believe in the possibility of complete and rapid cure.

Hurst, A. (1943) *Brit. med. J.*, **2**, 773.

SENESCENCE AND SENILITY

See also B.E.M.P., Vol. XI, p. 69; and Cumulative Supplement, Key No. 1394.

Normal old age

Expectation of life

Increasing longevity.—Bramwell from analysis of available recent statistics reaches the following conclusions on longevity. (1) Seventy years—the traditional span of life of the Psalmist—no longer holds good as the most common length of life of man. (2) The diagonal law persists for the ages 70, 80 and 90 years; so far as centenarians are concerned insufficient time has elapsed for a definite opinion to be given. (3) There is not any reason to suppose that the movement towards longer living has in any way spent itself; whatever happens to the population an increasing number of people for many years to come must be expected to survive to really great ages. It is difficult to assign a cause for this increasing longevity apart from generally healthier conditions and a gradual adaptation to town life. These changes do not affect directly eugenics at all; people of these ages are not concerned with begetting families. Indirectly they do affect eugenics very considerably; early death and early retirement lead to early promotion and this or its prospect in the not too dim future leads to early marriage and must result in larger families.

Bramwell, B. S. (1943) *Eugen. Rev.*, **35**, 8.

SEX HORMONES

See also B.E.M.P., Vol. XI, p. 90; and Cumulative Supplement, Key Nos. 1396–1398.

Source and constitution

Ovarian hormones and synthetic oestrogenic substances

Investigation with regard to reproductive cycle.—A series of ovaries were taken from adult female rats at various times when the ovulation period was accurately estimated, in an

investigation made by Dempsey and Bassett into the rapid changes which occur during the reproductive cycle. The ovaries were used for fluorescence and birefringence tests. Two general types of birefringence were observed, one in which the connective tissue of the ovary was weakly birefringent and the other in which strongly birefringent crystals were seen in certain cells of the ovary. Autofluorescence revealed a number of varying structures. The Graafian follicle emitted a blue colour of moderate intensity. The theca interna showed as strong white or bluish-white. Corpora lutea showed mottled blue and white areas. These experiments help to solve the problem of the relation between the ovarian lipoids and the steroid hormones of the ovary. It has been suggested that the granulosa cells elaborate the ovarian hormones; the theca interna has also been suggested because more hormone can be extracted from theca-cell tissue. Dempsey and Bassett consider that their experiments point to the theca rather than to the granulosa as the secretory cells for oestrogens. The essential difference between the fluorescence spectra of the theca and of the granulosa is that there are more of the longer wave lengths in the former. The difference is associated with the presence of fat-soluble substances in the theca. The experiments showed the presence of large quantities of steroids in degenerating follicles, in corpora lutea and in interstitial cells. The amounts of the reacting substances in the different structures varied according to the stage of the reproductive cycle of the ovary.

Corpus luteum hormone

Properties of relaxin.—Although both oestrogen (alone or with progesterone) and relaxin relax the pelvic ligaments, Abramowitz, Money, Zarrow, Talmage, Kleinholz and Hisaw disprove the identity of relaxin with either of the former. Commercially progesterone is extracted from corpora lutea with methanol. The residue, defatted and partially dried, is pressed into pellets and extracted with hydrochloric acid. To this emulsion, purified with sodium chloride, neutralized and filtered, is added ammonium sulphate, which precipitates a flocculent substance. This, collected by filtration, dialyzed and dried, contains one guinea-pig unit of relaxin per milligram. One unit of hormone produced symphysial relaxation in 6 hours in two-thirds of the number of the experimental animals used. Each milligram represents 1 gramme of fresh corpus luteum. In experiment, spayed guinea-pigs received 4 daily injections of oestradiol. On the fifth day animals which showed a relaxed pelvis were discarded. The remainder received an injection of relaxin which represented either 1 or 2 grammes of corpus luteum. Pelvic relaxation ensued in 6 hours, or not at all, and disappeared within 24 hours. The larger dose produced positive response of longer duration. With graduated doses up to, but not exceeding, 2 grammes equivalent of corpus luteum, increased response corresponded with increased dosage. Other findings were that neither the animal's weight nor seasonal variations were relevant and that in the absence of oestrogen relaxin is inert. The associated elements in the production of relaxin were found to be destitute of loosening powers, which demonstrates its specific action. Whereas relaxin is water-soluble, oestrogen and progesterone are not so and physiologically the effect of oestrogen in vaginal smears is not produced by relaxin. The individuality of relaxin appears indubitable.

Use of sex hormones in treatment of menstrual and climacteric disorders

Preparations and standardization of female sex hormones and gonadotrophic hormones

Octofollin.—Hufford, Roberts, Loeffel and MacBryde report on a clinical and experimental study of a synthetic oestrogen now named octofollin (2-4-di(*parahydroxyphenyl*)-3-ethyl hexane) and compare its action to that of the well known synthetic oestrogen stilboestrol. Eighty-one women who were suffering from oestrogen deficiency in connexion with natural menopause or artificial menopause as a result of operation, were treated. Included in the series were 3 who suffered from primary hypogonadism. All complained of severe symptoms of vasomotor instability. In some cases the new drug was given by mouth, in others by deep intramuscular injection and suspended in oil. The results were estimated by the amelioration of the symptoms and by vaginal smears before and after medication in every case, and hepatic function studies before and after treatment were made in the case of 13 patients. Repeated urine examinations were made in all cases. The results indicate that octofollin is effective in the treatment of hypogonadal symptoms in women and is relatively non-toxic. The effective dosage is however from 5 to 10 or even 15 times that of stilboestrol. It costs more per milligram than does stilboestrol and is therefore an expensive medication. It is said to be less expensive than are natural oestrogens.

Mode of administration and dosage

Methods adopted for various conditions.—Smith discusses the value of hormones in the treatment of functional gynaecological disorders. Thyroid extract is recommended but the mechanism by which its effect is achieved is obscure. Stilboestrol is of use but reports indicate that oestrone sulphate may be a more satisfactory oral oestrogen. The gonadotrophins give uncertain results and undesirable reactions. It is suggested that amenorrhoea be treated by the oral administration of stilboestrol 1 milligram every morning for 35 days before intramuscular injections are given of progesterone 10 milligrams daily for 5 days. A flow will probably ensue 2-5 days later. Modified courses are subsequently repeated until spontaneity of flow is discernible. Smaller doses of stilboestrol may be effective in the treatment of premenstrual disturbances, sterility and menopausal abnormalities. Induced endometrial bleeding at the climacteric is avoided by keeping the daily dosage below 0.5 milligram. Severe headaches associated with menstruation are relieved by 1 milligram of oestradiol dipropionate

injected intramuscularly 7 days before the expected onset of the menses. Midmonth pain and bleeding react favourably to thyroid medication or to methyl testosterone 5–10 milligrams given orally daily, except during menstruation. Inconsistent results follow the use of hormones in the treatment of dysmenorrhoea. For profuse or prolonged menstruation coming at intervals of about 28 days progesterone 10 milligrams and oestradiol benzoate 1 milligram are injected intramuscularly on the twenty-first day, and afterwards 4 daily injections of progesterone 10 milligrams are given. Three cycles of this therapy should be adequate. Daily doses of methyl testosterone 10–20 milligrams may be effective for frigidity but hormones are not usually indicated in the treatment of vulvo-vaginal disorders. Vaginal insertion of stilboestrol 0.5 milligram is occasionally employed for persistent senile vaginitis.

Methods of control

Two methods of estimating ovarian function.—Neustaedter and Mackenzie discuss the method of estimating ovarian function and the result of hormone therapy by vaginal smear as compared with the study of the endometrial pattern. Their observations of the smears during the menstrual cycle show that there are 6 phases in the vaginal secretions—postmenstrual, preovulatory, ovulatory, postovulatory, premenstrual and menstrual. The cytology of such a smear is difficult to evaluate, although in cases with oestrogenic deficiency the cytology is more definite. The smear method is not ideal for diagnosing ovulatory menstruation, but collection of the specimen is easy and free from risk and the method is applicable to virgins. For endometrial biopsy the authors used a cannula curette, with strict asepsis. The tissue specimens are fixed in Buoin's solution embedded in paraffin, cut, mounted and stained. The endometrial specimen shows the presence or absence of progesterone and thus gives reliable information about ovulation. The section may not, however, give a true uterine picture because of the different histological patterns which may be present in the uterus. Again, a biopsy cannot help to determine the exact time of ovulation. Biopsy is contra-indicated in pregnancy or in pelvic disease.

Clinical use of male sex hormone

Therapeutic uses

Experiments made on female monkeys.—Hisaw describes observations made on the effect of androgens on the reproductive organs of the female monkey, *Macaca mulatta*. Fifteen adolescent animals and one adult were used in the experiments. Preliminary castration was carried out in all but 6 which were sexually immature. Each monkey was given 1,000 international units of oestradiol daily for 30 days or longer, administration being stopped when they were menstruating; they then received daily injections of testosterone or testosterone propionate for 5 days. The results of the experiments furnish additional evidence that the androgen has a weak progesterone-like action. In doses of 2 milligrams testosterone propionate inhibited oestrogen-withdrawal bleeding for at least 20 days, the equivalent dose of progesterone being 1 milligram. Testosterone propionate appeared to be about 3 times as active as testosterone. For the purpose of precipitating bleeding in animals which were receiving oestrogen 1,000 international units daily, one injection of 1 milligram of progesterone was found to be as effective as were 9 milligrams of testosterone propionate given daily for 5 days. Testosterone is, like progesterone, capable of reversing the changes in the cervix, vaginal mucosa and skin of the sexual organs which are produced by oestrogen, but again much larger doses are required in order to achieve the effect. Unlike progesterone, testosterone did not act as a synergist with oestrogen in promoting uterine growth.

Abramowitz, A. A., Money, W. L., Zarrow, M. X., Talmage, R. V. N., Klein-

holz, L. H., and Hisaw, F. L. (1944) *Endocrinology*, **34**, 103.

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J. Amer. med. Ass., **123**, 259, 261.

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SHOCK AND COLLAPSE

See also B.E.M.P., Vol. XI, p. 126; and Cumulative Supplement, Key No. 1400.

Hypotheses of shock

Neurogenic hypothesis

Old theories challenged.—Phemister, Laestar, Eichelberger and Schachter state that the present-day explanation of shock from injury is that excessive afferent depressor nerve impulses are set up either in the wound or in the cerebrum, and that these cause a fall in blood pressure. The prolongation of this state is thought to result in complete circulatory failure and death. The term, primary shock, has been used to describe the condition. The authors consider it to be improbable that primary shock would be produced in this way. Experiments were made on more than 150 large rabbits. Stimulation of the aortic-depressor nerve maintained blood pressure at shock levels. Severe and prolonged lowering of blood pressure was produced first by bleeding to shock levels and then by stimulating the aortic-depressor nerves by electric currents of various strengths. In a few minutes the blood pressure was reduced to

low levels and the heart beat slowed. Removal of the stimulus resulted in rise of blood pressure to almost the previous level and by acceleration of the pulse rate. Respirations were hardly affected by the stimulation. Continuous stimulation resulted in lower blood pressure levels, the pressor response on release of the stimulus gradually weakened and the animal died. The blood usually became diluted, as was shown by reduction in erythrocyte, haematocrit, haemoglobin, plasma protein, oxygen and carbon dioxide content. After death some of the organs were found to be congested and there were acute degenerative changes in the liver and kidneys. Direct stimulation of the somatic nerves in a single area (as in a simple injury) produced only a slight lowering of blood pressure of short duration. These effects were produced by exposure and stimulation of the somatic nerves by pinching or crushing or by the use of electric currents of varying strengths. One of the authors had previously noted that manipulations during upper abdominal operations produced a temporary fall in blood pressure, which may be the result of afferent depressor nerve impulses. Low blood pressure, either in syncope or from abdominal manipulations, if combined with a low blood pressure from haemorrhage, might produce shock.

Loss of body fluid

Fainting among donors.—Barcroft, Edholm, McMichael and Sharpey-Schafer state that vasovagal fainting reactions with acute fall of blood pressure and slow pulse demand detailed study because they constitute one manifestation of oligæmic shock. Fainting occurs in 3·8 per cent of donors from whom 440 cubic centimetres and 8·5 per cent of donors from whom 540 cubic centimetres of blood have been drawn. Of those bled to the extent of from 800 to 1,000 cubic centimetres 11 out of 28 fainted, and of donors bled to the extent of from 1,000 to 1,200 cubic centimetres 15 out of 29 fainted. Observations were made on healthy young male volunteers in the supine position about 2 hours after they had taken lunch. Bleeding was carried out by venesection, or similar effects were produced by placing venous tourniquets on the thighs at diastolic pressure for about 20 minutes and then drawing off a small quantity of blood. During fainting after haemorrhage, cardiac output (measured by a direct Fick method) and right auricular pressure (measured by cardiac catheterization) were often substantially unchanged. The acute fall in blood pressure could not be explained by bradycardia and decreased cardiac output and it was therefore taken to be due to peripheral vasodilatation. Forearm blood flow during the faint was approximately doubled and since the blood pressure was about halved this phenomenon indicated pronounced vasodilatation. The site of vasodilatation was found not to be the skin, which was pale; the data pointed to the arterioles of the underlying muscle of the forearm as the site. If vasodilatation of the same order occurred throughout the body musculature there would be a marked drop in the blood pressure, possibly great enough to explain the fall in pressure during fainting. The authors state that vasodilatation was mediated by vasomotor nerves. The authors' data do not support Lewis's suggestion that the similarity between the vasovagal syndrome and the effects of stimulation of the carotid sinus (cardiac slowing and fall of blood pressure) might be explained by assuming that the same central and efferent mechanisms were involved in both cases.

Toxaemia

Experimental data.—Local loss of fluid, toxaemia or neurogenic phenomena are the theories of the cause of shock which are now supported. Prinzmetal, Freed, and Kruger describe 8 experiments which support the toxaemia theory. Attempts in experiment (1) failed to produce shock in dogs by means of rifle bullet wounds of the hind leg. In experiment (2) the quadriceps muscle was aseptically excised, crushed and replaced. Shock, usually fatal, ensued invariably although local fluid loss never exceeded 3 per cent of the body weight. In experiment (3) the procedure was repeated without muscle crushing and shock was absent. Since the nervous stimulus was identical in both experiments, the neurogenic origin of shock is discounted. The crushed muscle procedure was repeated in experiment (4) with removal of the crushed tissue in order to stimulate debridement, within 17 hours, and recovery generally ensued. Such debridement after 24 hours generally failed. When the products of a debridement performed within 4 hours were surgically inserted into the contralateral hind leg 4 days later, shock ensued. The deduction is made that crushed muscle is responsible for shock and the principle of debridement and its earliest possible performance is vindicated. In experiment (5) the crushed muscle procedure of experiment (1) was followed by the application of plaster splints for the purpose of constraining local exudation. Their application did not exclude shock and the theory of local fluid loss as a cause of shock is thereby weakened and that of toxaemia supported. Bacteriological studies, which constituted experiment (6), showed widespread bacterial contamination of the crushed muscle at necropsy. The authors suggest consideration of bacterial action, the action of katabolites of crushed muscle and of toxins elaborated by their interaction as toxic factors in the causation of shock. Experiment (7) showed that saturation of the crushed muscle with antiseptics before its replacement prevented the development of shock. Similarly, experiment (8) showed that the oral administration of sulphamerazine (2-sulphanilamido-4-methyl-pyrimidine) before and after operation prevented shock. Apparently bacterial action rather than muscular katabolites is responsible. Finally, compression by plaster splints is applicable as a preventive of acute shock which results from fluid loss, but the shock condition here described was toxic in character and was relieved only by debridement.

Six groups defined

Review of certain aspects of shock.—In an address on Medicine before the Royal College of Physicians and Surgeons of Canada, Meakins gives his own interpretation of the state of shock. The unrelated and often uncorrelated signs and symptoms are impressive but confusing and are divided into 6 groups—nervous, cutaneous, gastro-intestinal, circulatory, respiratory and haematological. The first 5 groups are usually present to some extent but blood changes may or may not occur depending upon whether or not there has been whole blood loss. The emphasis placed upon the importance of this finding has led to much confusion which has been assisted by the numerous adjectives appended to the term shock, such as surgical, secondary, haemorrhagic, traumatic, dehydration. These serve only to indicate that a serious, even fatal, condition may follow. There has been a constant cry for a sign to indicate when shock is impending but Meakins does not believe that any such an index can be formulated; shock is an extremely insidious progressive state which must be expected in many diverse conditions and indeed often occurs without detection. The clinical signs due to shock are fluid loss, tissue ischaemia, systemic intoxication and dehydration. The really uncomplicated cases of haemorrhage occur from the gastro-intestinal tract, occasionally from the lungs. In practically all other instances there is the probable complicating factor of trauma. It should be quite obvious that haemorrhage should be met by whole blood substitution therapy. Shock due to burns is almost a unique condition most comparable with the choleraic diarrhoeas and is due to loss of plasma. Crushing injury is a more complicated phenomenon and is nearly always accompanied by whole blood loss, which must be made good.

Treatment*General*

Importance of the resuscitation team.—The chief clinical components of shock in war injuries are divided by McMichael into (1) oligæmia (deficiency from loss of blood) and its sequelae, (2) renal failures, (3) burns and (4) complicating factors such as infection. Oligæmia resulting from shock occurred in 90 per cent of the author's 200 observed cases of shock in air-raid casualties. The treatment consists in the giving of transfusions, in rest and in ensurance of enough warmth for comfort. Morphine is not required until the shock is passing off and the patients complain of pain. For transfusion, blood is the best fluid, but serum or plasma may be used equally well provided much haemodilution is not caused. The use of serum saves time in urgent cases. McMichael believes that in cases with blood pressure below 90 persisting for one hour, transfusion is required; it may be given as quickly as fluid will run into the veins, and must be continued until blood pressure is normal; thereafter drip transfusion should be maintained until after operation. Oxygen therapy is not always practicable. Vasoconstrictor drugs are usually unsuitable, but the N-methyl derivative of amphetamine (methedrine) may be of value in post-operative cases with loss of arteriolar tone. Failure of therapeutic measures may be due to continued haemorrhage, pulmonary fat embolism, bacterial infection, pre-existing disease, carbon monoxide poisoning or the irreversible state. The organization of resuscitation teams is most important for that continuous care which is necessary in cases of shock after war-time injuries. Students, nurses and orderlies may participate in them.

Heat application

Need for strict control.—There are published observations which show that the indiscriminate application of heat to patients with shock may not be the best routine procedure to follow. Wright and Devine investigated 19 patients with this in mind, 17 of whom had traumatic shock, one had shock after administration of a mercurial diuretic and one after a rapid haematemesis. The authors consider that a drop in internal temperature is not usual in cases of shock, but that if the patient is exposed to a low environmental temperature, the internal temperature falls as readily as does that of normal persons in similar circumstances; the mouth temperature however is often lower than in normal persons. In some cases in which no heat was applied after admission to hospital and in which the patients were merely covered with blankets, rectal temperature rose well above the normal limits. The authors make the following recommendations. (1) Heat should not be applied to patients with shock until the rectal temperature has been taken; repeated observation of rectal temperatures will guard against harmful overheating. (2) Heat should not be applied to a shocked patient unless facilities are at hand to supplement the loss of circulating blood which occurs as a result of change from peripheral vasodilatation to vasodilatation. (3) Radiant heat cradles need close supervision when used in the treatment of shocked patients and probably should not be allowed to raise the air temperature above 90° F. The shocked patients who were studied showed a pronounced increase in the normal difference that exists between rectal and oral temperatures; the average difference was 2.6° F. in the shocked patients and 1.1° F. in controls.

Isinglass as a substitute for blood in transfusion

Taylor and Moorhouse expound the biochemical suitability of isinglass as transfusion material in haemorrhage and shock and Pugsley and Farquharson describe its clinical application. Dried hake sounds provide an inexhaustible supply of this collagen. The criterion of efficient transfusion is the restoration and maintenance of blood volume until fluid is physiologically substituted. In the investigation of haemorrhage 28 dogs were bled until the blood pressure fell to 25 millimetres of mercury. From 47 to 71 per cent of the total blood, estimated by the haematocrit immediately before and after isinglass injection, was abstracted. The haemorrhage, if transfusion had not been made, must invariably have been fatal. A

solution of isinglass 4 to 6 per cent, equivalent to the blood loss, was rapidly infused. Three dogs succumbed before transfusion and 6 during or soon after; 19 recovered completely. In artificial traumatic shock transfusion of blood amounting to 50 per cent of the calculated blood volume of the shocked animal produced sharp rise in blood pressure, then sharp fall and return to shock level. The average survival time was 60 minutes. Similar transfusions of isinglass produced a remarkable but not a sustained response with an average survival of 120 minutes. Taylor has no satisfactory explanation to offer of these disappointing results. Isinglass proved to be free from antigenic action. Autoclaving and improved filtration now produces isinglass which has a pyrogenic action below 0.5° F. Regeneration of plasma protein is encouraged rather than inhibited and the increase of blood sedimentation rate is negligible. In hospital 4, 6 and 7 per cent concentrations of powdered isinglass in physiological saline solution were administered. The average dose of 300 cubic centimetres was administered by the drip method, doses of 25 cubic centimetres by syringe. In 51 subjects selected for hourly observations during and after transfusions the first 34 administrations produced mild pyrexia in 8 cases; 24 subsequent administrations of an improved preparation produced a febrile reaction in 3 cases. Severe reactions were absent. In all patients treated response was excellent. These included 3 cases of haemorrhage, 3 of burn shock and 2 of shock from compound fracture. Two further patients with circulatory failure, although they ultimately succumbed, had improved with isinglass transfusion.

Oral sodium lactate

In burn shock.—Fox gives an account of the use of oral sodium lactate in the treatment of shock due to burns. In a group of cases of thermal burns morphine was given when the patients were admitted to hospital and blood samples were taken for analysis. Chilled isotonic sodium lactate solution (1.75 per cent concentration) was given orally in quantities of from 10 to 15 per cent of body weight, ranging from 7 to 10 litres (12½–17½ pints), during the first 24 hours. The burned areas were dressed with neutralized tannate-sulphadiazine ointment with a pH of 7.6. The amount of sodium lactate solution administered was recorded, and blood pressure estimations and samples of blood were taken at short intervals during the first 24 hours. The urinary output was measured, and the administration of fluid was regulated to obtain from 1 to 2 litres of urine daily. If vomiting occurred more fluid was given. In some cases the solution was given by intranasal drip feed. A high protein diet was supplied and in severe cases amino-acids were also given. The blood samples were analysed for relative cell volume and for plasma constituents. In the author's group of unselected cases the 'shock' blood pressure approached normal levels while the haematocrit findings were still high. In cases in which there was considerable oedema there was little surface oozing. The large volumes of fluid given seemed to be well tolerated and the results were very successful. There was only one death (which occurred within 4 hours of the patient's admission to hospital) in 17 cases of full thickness burns. Further studies on the utilization of sodium in the body during shock are being made. Administration of a suitable mixture of plasma with sodium lactate might be more efficacious than that of sodium lactate alone.

Pectin

The value of pectin 1.5 per cent in Ringer's solution or in sodium chloride solution infused in the treatment of shock is assessed by Meyer, Kozoll, Popper and Steigmann. The solution employed for 60 patients, which possessed an oncotic pressure slightly in excess of that of plasma and a viscosity less than that of whole blood, was buffered to a hydrogen ion concentration of 7.2 with sodium phosphate. Shock which displayed decrease in systolic blood pressure up to 50 millimetres of mercury was classified by the authors as mild or moderate, if it exceeded 50 millimetres, as severe; pulseless conditions were designated profound shock. The blood before and after the infusion was investigated for comparison of sedimentation rate and for the content of haemoglobin, plasma protein, nitrogen and the haematocrit reading. In 27 cases of mild and moderate shock and 9 cases classified as severe or profound a single infusion of 1,000 cubic centimetres of pectin solution proved to be effective. Six patients were effectively relieved of shock, moderate to profound, but later had to have a transfusion of whole blood in order to combat anaemia. In 3 cases a pectin infusion did not produce immediate recovery and in 3 other patients shock was overcome but death ensued from the underlying disease. In 4 cases, 2 of which were of mild or moderate shock and 2 of profound, blood succeeded where pectin failed, and in 8 patients, of whom 5 were already moribund, pectin infusion was without effect. Clinically the average blood pressure of 74/43 improved after infusion to an average of 107/68 and was sustained, with improved pulse rate and volume. Temperature and respiration were little affected. The change from a cold clammy skin to a warm and dry one was outstanding. The diminished haematocrit count, haemoglobin, plasma density and nitrogenous content which were recorded immediately after the infusion were found to be progressing towards correction within 24 hours. A prolonged elevation of the blood sedimentation rate, the only adverse phenomenon, proved to be clinically harmless. Repetition of pectin infusion is unavailing; although it cannot displace whole blood transfusion it may prove to be valuable in emergency.

Barcroft, H., Edholm, O. G., McMichael, J., and Sharpey-Schafer, E. P. (1944) *Lancet*, 1, 489.

Fox, C. L. (1944) *J. Amer. med. Ass.*, 124, 207.

McMichael, J. (1944) *J. Amer. med. Ass.*, 124, 275.

- Meakins, J. C. (1943) *Canad. med. Ass. J.*, **49**, 21.
 Meyer, K. A., Kozoll, D. D., Popper, H., and Steigmann, F. (1944) *Surg. Gynec. Obstet.*, **78**, 327.
 Phemister, D. B., Laestar, C. H., Eichelberger, Lilian, and Schachter, R. J. (1944) *Ann. Surg.*, **119**, 26.
 Prinzmetal, M., Freed, S. C., and Kruger, H. E. (1944) *War med.*, **5**, 74.
 Pugsley, H. E., and Farquharson, R. F. (1943) *Canad. med. Ass. J.*, **49**, 262.
 Taylor, N. B., and Moorhouse, Margaret S. (1943) *Canad. med. Ass. J.*, **49**, 251.
 Wright, R. D., and Devine, J. (1944) *Med. J. Aust.*, **1**, 21.

SILICOSIS

See also B.E.M.P., Vol. XI, p. 133; and Cumulative Supplement, Key No. 1401.

Aetiology

Industrial processes

Aluminium dust in treatment of early silicosis.—Heffernan divides the harmful dusts met with in industry into two classes, (1) organic and (2) inorganic. Organic dusts can be subdivided into living and non-living. Non-living organic dusts can cause allergic reactions in sensitive people; the living dusts may cause fungus infections of the lungs, of which the best known is actinomycosis. Inhalation of inorganic dusts may cause fibrotic changes in the lung. Such dusts vary in harmfulness, silica being the most harmful. Siliceous dusts act by combining with the protoplasm of the cells whereas the non-siliceous dusts exert a mechanical action only, blocking lymphatic drainage channels and glands. The prevention of dust fibrosis in industry depends upon removal of dust from the air which reaches the lungs. Wet processes should be substituted for dry whenever it is possible, special methods of ventilation should be installed and, as a last resort, specially designed masks should be worn. Experiments on animals indicate that silicosis of the lung does not develop if aluminium dust is simultaneously inhaled. Researches now in progress should decide whether or not aluminium dust can be successfully used in human beings as a preventive or cure of silicosis. Results already obtained encourage the hope that early silicosis may become arrested or even undergo partial resolution under treatment with aluminium.

Clinical picture

Symptoms and signs

Silicosis and tuberculosis.—Auerbach and Stemmerman state that published work has hitherto presented a picture of silico-tuberculosis in which the phthisis is described as unique and as an important factor in the development of the silicotic nodule. The authors cannot confirm these findings from their own necropsy material, which is almost entirely derived from patients with tuberculosis. In the course of their routine necropsy examinations they found 63 cases of silicosis, in 54 of which the patients had an associated chronic pulmonary tuberculosis. The other 9 cases of silicosis (found in a tuberculosis institution) provided no evidence of tuberculosis even after careful histological examination. The findings in the 63 silicosis cases are compared with those in 200 unselected cases of chronic pulmonary tuberculosis. The authors find that although silicosis and tuberculosis exist concomitantly in the same lung each maintains its own character. The tuberculosis alters the silicosis not at all. The pneumoconiosis alters the tuberculosis only in so far as the silicotic nodules prevent the full development of tuberculous granulation tissue and of the pyogenic membrane in the walls of cavities. Both granulation tissue and pyogenic membrane however are present in those parts of the lung in which the silicotic foci are small or absent. The size, situation and number of cavities are much the same. There is a slightly greater incidence of perforation of cavities through the interlobar fissures in the silicotics and a greater incidence of fatal pulmonary haemorrhage. It is difficult to determine the exact time at which pulmonary tuberculosis is superimposed upon pneumoconiosis, unless the patient has been under observation in the transition period, as the symptoms of the two diseases are so similar. Whereas fever and proof of cavitation are useful diagnostic aids the final conclusion must be based upon the demonstration of the tubercle bacillus. Collapse therapy is of little value in silico-tuberculosis, apparently because the silicotic lung remains voluminous and shows no tendency to collapse. Most of the authors' patients succumbed to progressive pulmonary insufficiency.

Radiological and histological appearances

In haematite iron-ore workers.—Fawcitt discusses the radiological evidence found on examining the chests of haematite iron-ore workers in the Furness and South Cumberland regions of the English Lake District. The modern era of treatment may be said to have begun with Haldane, with whose general views Fawcitt is strikingly in agreement. He points out that the snowstorm radiograph usually regarded as typical of classical silicosis may be exactly duplicated in a haematite miner because of the opacity of the deposits of haematite dust in the lung tissue, without the presence of any pulmonary fibrosis or any untoward symptoms. Thus there is no such thing as X-ray diagnosis of industrial disease of the lungs—there is only X-ray evidence, which sometimes may be misleading. At one time it was thought that haematite dust *per se* did little harm. But haematite fibrosis is now compensated for since the Silicosis Act was amended in 1935. True silicosis and silico-siderosis are or were prevalent

in the Cumberland iron-ore miners but are not found in Furness. This fact Fawcitt attributes to the use of dry compressed-air drills and to the higher silica content of the Cumberland ore. His description of mixed types of fibrosis, including the infected types, run on accepted lines and he emphasizes the influence of micro-fungi and of the tubercle bacillus in alteration in the type of the condition.

Auerbach, O., and Stemmerman, Marguerite G. (1944) *Amer. Rev. Tuberc.*, **49**, 115.

Fawcitt, R. (1943) *Brit. J. Radiol.*, **18**, 323.

Heffernan, P. (1943) *Brit. J. phys. Med. N.S.*, **6**, 135.

SIMMONDS'S SYNDROME

See also B.E.M.P., Vol. XI, p. 145.

Treatment

Pituitary transplantation

The therapeutic possibilities of pituitary transplantation in Simmonds's disease are discussed by Marti, who has performed the operation in 3 cases, using calves' pituitaries. Laparotomy was carried out under local anaesthesia. Two freshly excised glands were sewn into a pocket in the omentum and a third was imbedded in the subperitoneal fat. The author's conclusions from these cases are as follows. (1) In severe cases of Simmonds's disease which do not respond to ordinary hormone therapy, pituitary transplantation can produce notable, although possibly only temporary, improvement. Up to four years after treatment the authors' patients remain greatly improved, enjoy life and are able to work. (2) It is essential that the implanted material be freshly excised under aseptic conditions. Omental transplantation appears to offer the best chance of survival of the grafts. (3) Administration of preparations of the anterior lobe of the pituitary gland and of the adrenal cortex should be maintained during the period before the graft has assumed its functions.

Marti, T. (1943) *Schweiz. med. Wschr.*, **73**, 1357.

SKIN DISEASES: AFFECTIONS DUE TO INSECTS AND ACARINES

See also B.E.M.P., Vol. XI, p. 149; and Cumulative Supplement, Key Nos. 1403 and 1404.

The occasional attacker

Acarines

Grain itch.—Rogers reports on an epidemic of grain itch in Phoenix, Arizona. The disorder is due to a mite known as *Pediculoides ventricosus*. The mite lives as an ectoparasite on various insects especially in their larval stages and the most common of these is the grain moth. The lesion of the skin, microscopically examined, showed that the mite does not burrow into the skin as does the acarus of scabies; the pathological changes in the skin are characteristic of urticaria. No trace of a puncture can be discerned. The disease appears to be fairly common in certain farming districts of the United States of America but many cases are not diagnosed since the condition responds to simple remedies. There are several synonyms for the disorder: acarodermatitis urticarioides, barley itch, grain mite dermatitis, straw itch, mattress itch and hay itch. It is thought that the pediculoides in the process of abstracting liquid substance from the skin synchronously injects an irritating substance which gives rise to an urticarial eruption. These lesions may be situated anywhere in the body and are extremely itchy. They are from pale pink to bright red in colour and vary from pin-head size to 2 or more inches in diameter. Many lesions are surmounted by a tiny vesicle. Secondary infection is common as a result of scratching and pyoderma and impetiginous lesions may occur. Moderate leucocytosis and eosinophilia have been reported, with occasional albuminuria. Slight malaise is present only when the lesions are very extensive or when positive secondary infection occurs. Diagnosis is indicated by a history of previous contact with straw and the occurrence of the eruption in families or in groups of labourers. Since the mite remains attached to the skin for only a short time, remedies for relieving the subjective symptoms are all that is necessary. Dusting of the buildings and the granaries and of other material that comes in contact with grain and straw with powdered sulphur has been recommended as a means of getting rid of the mite. Rogers describes three successive outbreaks of grain itch which occurred in men who handled bales of hay for the same company between 1941 and 1943. Allergy to hay and to insect bites were among the suspected causes but the aetiology was elucidated by the demonstration of *Pediculoides ventricosus* in samples of the hay examined.

Parasites breeding on human host

Animal scabies in the human

Study of life cycle.—No reliable account has yet been given of the complete life cycle of any burrowing mite concerned in the transmission of scabies in human beings and animals; Gordon, Unsworth and Seaton have therefore studied the development and transmission of scabies infection in rats and have investigated minutely the life cycle of a burrowing mite commonly found in animals, namely *Notoedres cati*. A smaller number of experiments were subsequently carried out with *Sarcoptes scabiei* and although the two species differ biologically it is probable that the methods which prevent and cure *Notoedres* infections in rats will be

equally effective in the treatment of scabies infection in man. In white rats infected by *Notoedres* the larvae hatch out from eggs after 4 or 5 days' incubation in the skin burrows; most of the larvae continue to develop within the burrows until the first nymph stage is reached, when they usually pass to a new site to attain the second nymph stage. No evidence was obtained that the larvae of *S. scabiei* enter the skin through the hair follicles, as has been suggested in the literature. Within a period of about 2½ weeks between the hatching and the final moult of *Notoedres*, the adult male and female organisms are formed. The adult males emerge from the skin tunnels and move about on the skin surface in search of females. The female lies in the skin burrows until fertilized by a male which shows great discrimination in the penetration of burrows containing only mature females. After copulation 4 or 5 days intervene before the eggs are laid. The female extends the tunnel and deposits about 3 or 4 eggs a day up to a total of about 50 eggs. The average duration of life for the adult female is probably 3 or 4 weeks, most of which is spent below the skin surface. The disease spreads from host to host chiefly by the migration of the miniature larvae and nymphs. In any individual host secondary reinfection also may occur as a result of scratching which deposits organisms in fresh areas. In human scabies transmission probably occurs mainly by transference of the larval forms and to a lesser extent by nymph organisms, although other observers still hold different views.

Gordon, R. M., Unsworth, K., and Seaton, D. R. (1943) *Ann. trop. Med.*

Parasit., **37**, 174.

Rogers, G. K. (1943) *J. Amer. med. Ass.*, **123**, 887.

SKIN DISEASES: OCCUPATIONAL DISEASES

See also B.E.M.P., Vol. XI, p. 161.

Dermatitis

Causes

Contact dermatitis in aircraft workers.—Hall considers dural, aluminium or metal poisoning to be terms too narrow to cover the contact dermatitis which affects aircraft workers. He analyses 202 cases. Zinc chromate primer, the dull green coating to metal sheets and parts of aeroplanes during manufacture, accounted for 132 cases, aluminium for 4 and its alloy, duralumin, for 10 cases. Operatives who are even casually concerned are liable to sensitization. Other identified irritants, notably soap powder and spun glass, provided 47 cases and contacts not identified but presumed to be industrial provided 9 cases. Patch tests for each suspected ingredient of the primer—zinc chromate, a phenolformaldehyde and a natural resin, with phthalic anhydride—were devised. Thereby the types of dermatitis peculiar to each were identified. After this identification a disk coated with the whole primer sufficed as patch test for each case. It was ascertained that cases of dermatitis confined to hands and arms, when positive to the disk test, were due to chromates. In cases similarly positive, dermatitis of the eyelids, neck and antecubital fossae were due to one of the resins. When patients showed a dermatitis which combined these distributions and had a positive disk test, their sensitivity applied both to chromates and resins. Transference to work which does not involve contact with the irritant is essential to recovery. Any erythematous or papular rash of the forearms suggests the application of a patch test with aluminium or dural particles. A positive reaction of 24 hours' duration is diagnostic and indicates that transference to occupation free from such contacts is imperative. Immunity does not develop among workers in these materials but systemic manifestations are absent. Spontaneous healing is the rule, aided by soothing applications and, rarely, by superficial X-ray irradiation.

Review of one thousand cases.—A study of 1,113 cases of various skin diseases, including 527 cases of occupational dermatoses, has been made by Klauder for the purpose of ascertaining the most important causal factors. Nine hundred and nine of the patients were men and 204 were women. In the non-occupational group of 586 cases the most common skin diseases were eczematous dermatitis, tinea of the extremities, pyoderma, pityriasis rosea, miliaria, seborrhoeic dermatitis, lichen planus, urticaria, herpes zoster and erythema multiforme; syphilitic lesions, pemphigus vulgaris and lupus erythematosus also occurred. In the group of 527 non-occupational cases the causes were classed as (1) trauma and accidental injury (131), (2) primary non-aqueous irritants (128), (3) cleansing agents used on the skin (128), (4) sensitizing substances (66), (5) petroleum products (45) and (6) wet work (water, soap and water and alkalis) (48). Other observers have pointed out the importance of alkalis, lime, cement, metal pickling and other solutions, certain acids, chromium compounds, dyes and non-aqueous solvents in the production of occupational dermatoses. The author includes turpentine and other solvents among the common causal agents. (1) Trauma and accidental injury were the most common initiating causes and gave rise to 16 different types of lesion: pyoderma, dermatitis, ulcer of the leg, traumatic herpes zoster, alopecia areata, psoriasis, anthrax, erysiploid, sporotrichosis, keloid, pigmentation due to a burn, tattoo from metal filings, erythema multiforme after cellulitis, urticaria after an injection of tetanus antitoxin, traumatic avulsion of the hair, and insect bite. (2) Among the primary non-aqueous irritants were solvents, alkalis, chromic acid and chromic salts, pigments and dyes, paints, enamels, varnishes and acids; dermatitis was also caused by the use of formaldehyde, sulphur dioxide, creosote, copper sulphate and cyanates. (3) Irritant cleansing agents included soap, volatile

solvents, calcium hypochlorite and sodium hypochlorite solution, sodium cyanide, pumice and turpentine. (4) Substances which caused sensitization dermatitis were found to be petroleum products, anti-corrosion oils and linseed oil, insulation material, cashew nut oil and possibly pine oil, colouring ingredients, bakelite, chrysanthemum leaves and various wild plants, vanilla, cinnamon, insecticide, glue, methylaminocresol sulphate, methyl and ethyl acrylate, trinitrotoluene, permanent wave lotion, and scalp lotions. Solar erythema after contact with pitch was also observed. (5) Melanosis with epithelioma occurred in one patient who worked with mineral oil. Oil folliculitis is the most common eruption in men who work with lubricating oils; the syndrome is characterized by the presence of comedones, follicular papules, pustules, pyoderma and acne. Cases of folliculitis of occupational origin amounted to 21, comprising eruptions caused by chlorinated hydrocarbons, linseed oil, dust and glass wool. There was one case of interdigital erosion due to blastomycetes infection and one of recurrent herpes simplex in association with 'zinc chill'. (6) Wet work was responsible for dermatitis in 48 instances as a result of prolonged immersion in water and of exposure to soap preparations and to alkaline salt detergents.

Hall, A. F. (1944) *J. Amer. med. Ass.*, **125**, 179.

Klauder, J. V. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 579.

SKIN DISEASES: TUMOURS

See also B.E.M.P., Vol. XI, p. 200.

Innocent tumours

Derived from superficial layers of epithelium

Plantar warts successfully treated with formalin solution.—Thomson reviews the treatment of plantar warts with formalin and describes a simple and efficient technique. Early in 1939 the possible value of formalin was suggested by the 'accidental' cure of a woman who had numerous virus plantar warts over the soles of the feet; she also suffered from bromidrosis and was given 3 per cent formalin to relieve the latter condition. It was intended to give her X-ray irradiation treatment for the warts in 3 weeks time. When she returned after 3 weeks the warts had entirely disappeared, leaving punched-out holes. During the same year about 40 patients with warts were treated with the formalin lotion, and a large number were rapidly cured. It was soon seen however that there was considerable risk of causing eczema in all skin areas except those of the soles and palms. X-ray irradiation or radium had been used unsuccessfully in 8 cases. The majority of the lesions were of the virus type but in 6 cases the warts were single and appeared to be traumatic in origin. Most of the patients were seen several times and were kept under observation until the lesions disappeared and afterwards for a further period of from 2 to 3 months. The treatment failed only in 2 girls under 20 years of age. The technique used included the use of a 3 per cent aqueous solution of formalin; this was poured into a small saucer or plate so that the heel or fore part of the foot could be immersed in the solution without the thinner skin on the upper part of the foot being wetted. The part involved was soaked each night for 10 minutes. No other treatment was given. In most cases the pain disappeared after 7 or 10 days, and in 3 weeks' time the warts were white macerated plugs in the epithelium and could be easily scraped out with forceps. In a few cases from 7 to 8 weeks' treatment was required. It is suggested that other workers should give the method further trial and should report the results obtained.

Derived from hair follicles

Folliculoids as a cause of cancer.—Folliculoids are substances which possess an activity like that of the secretions of ovarian follicles. Whether natural, such as oestradiol, or artificial, such as stilboestrol, they penetrate the skin on inunction and produce in the mouse oestrus-like changes in the uterus. Although they are reputed to be carcinogens, Selye states that folliculoids have not been observed to produce cutaneous cancer. Observation has shown that injection of folliculoids into the rat's uterine lumen has readily produced precancerous changes. As folliculoids are often incorporated in ointments for use on the skin, reinvestigation seemed to be desirable. For investigation, the rhino mouse, which bears the allelomorph of the gene for the hairless mouse, was selected by Selye. Its skin, which is nearly hairless, is thickened and corrugated. The derma contains cysts most of which are filled with amorphous detritus. A few of the cysts contain cornified squamous cells. Those contiguous to sebaceous glands receive the secretions of the glands. The cysts are degenerated hair follicles, which when the skin is raised are visible as white granules. The resemblance to ichthyosis follicularis is noteworthy. In Selye's experiment a group of 4 mice received daily inunctions of oestradiol in peanut oil for a period of 4 months and a second group received inunctions of peanut oil only. There developed in the animals treated with oestradiol a layer of readily shed cornified epidermal scales and a thickened derma. The mice were killed and examined at the end of the 4 months. The white granules were magnified in the first group of animals. Histological examination showed great keratinous accumulation within the abnormal follicles. The sebaceous glands had almost disappeared, perhaps as a result of pressure. The corium showed vascular hyperdilatation. Abnormal production of keratinized material predominated. The overflow of this on the free surface of the skin formed the cornified epidermal layer which had been observed during life. Malignant changes were not observed.

Derived from nerve tissue (glomus tumour)

Symptoms and treatment.—Love defines the glomus as a normal constituent of the skin and

subcutaneous tissue; it develops during the first year of life and is concerned with the control of blood pressure and with heat regulation. From this tissue may arise the glomus tumour, an arteriovenous structure a few millimetres in diameter which contains nervous and muscular elements. Its origin is traumatic and its preferred site is the finger or toe, often under a nail. A visible glomus tumour is purple, with a liability to haemorrhage. Whether or not malignant changes may occasionally supervene is debatable. Intense paroxysmal pain radiating from the lesion is the outstanding feature and may pervade half the body, sometimes with hemiparesis and hemi-anaesthesia. If in diagnosis the pressure of a pin's point is gradually advanced to the painful spot indicated by the patient, the pressure is tolerated readily to within one centimetre of the lesion, but pressure over the lesion excites immediately the characteristic radiating pain. The severity of this phenomenon excludes neurofibroma, angioma, melanop-epithelioma and verrucose lesions. Simple excision, including when possible a good portion of surrounding tissue, effects complete but not necessarily immediate cure and of this probable delay warning should be given. When a subungual tumour is removed, the nail should not be trephined, as the hole will fill with serum and excite severe pain. The procedure recommended is to inject a little novocain into the site of maximum tenderness and to leave the needle in position for guidance. The injection for block anaesthesia is then made at some distance and the excision is performed.

Innocent infective conditions

Sarcoids

Besnier-Boeck-Schaumann disease (sarcoidosis).—The concept of sarcoidosis as a generalized systemic disease is reviewed by Katz, Cake and Reed who publish 10 typical case reports. Since 1914 it has been known that sarcoidosis, or benign lymphogranuloma, may involve any organ in the body and thus may give rise to many clinical manifestations; originally it was thought to be a disease of the skin characterized by granulomatous infiltration. The cause of sarcoidosis is obscure. Many observers consider that it is a benign type of tuberculosis because some recorded cases have terminated in frank tuberculosis, but tubercle bacilli cannot usually be demonstrated in sarcoid lesions and from 60 to 80 per cent of patients fail to show positive skin reactions to tuberculin. It is suggested by some workers that sarcoidosis may be caused by an atypical or non-acid-fast phase of the bacillus. According to Filho the entire sarcoid syndrome may be found in leprosy, but Longcope and Pierson were unsuccessful in an attempt to grow fungi from the lesions. Neutropenia and leucopenia suggest a virus agent and the presence of eosinophils in the blood stream in some cases suggests an allergic reaction. The pathological picture is characteristic and the lesions are identical in any structure. Clinically sarcoidosis generally consists of widespread involvement of one or more organs, with few constitutional manifestations. The onset is insidious and the course is usually slow with periods of remission. The commonest initial finding is enlargement of the lymph glands and pulmonary lesions are common. Bone lesions, which are found in from 10 to 20 per cent of cases, are chronic. The laboratory findings, course, diagnosis and treatment are discussed. Complete cure may occur and the prognosis is generally good unless vital organs are involved. Various methods of treatment have been advocated; carbon dioxide snow, X-ray irradiation and ultra-violet irradiation have been of value in some cases of skin involvement but up to the present treatment has remained empirical.

Systemic conditions

Innocent: xanthoma

Familial incidence.—Swanson describes an example of familial xanthomatosis. A variety of syndromes of faulty lipid metabolism are known in which deposition of cholesterol in the tissues occurs. Histologically, the lesions consist of connective tissue cells which are distended with droplets of cholesterol ester. The clinical picture depends upon the site of the process. Besides skin lesions, involvement of the membrane bones of the skull gives rise to the Hand-Schüller-Christian syndrome, and lesions of the cardiovascular and genito-urinary systems and of gall-bladder, liver, spleen, and choroid plexus are known. The presence of hypercholesterolaemia is common but not invariable. The skin lesions are of three types—xanthoma palpebrarum, xanthoma tuberosum, and xanthoma diabeticorum. Swanson's patient was 72 years of age and the backs of her hands were covered by large firm tumours, with similar swellings on wrists, elbows, right buttock, legs and ankles. Xanthoma palpebrarum was conspicuously present. Blood cholesterol was 298 milligrams per cent. The patient was sent into hospital for biliary colic and on cholecystectomy the gall-bladder was found to be filled with mixed stones. Histological examination showed xanthomatosis of the gall-bladder. The patient was one of a family of 6 sisters and 5 brothers; one brother had yellow lumps on the arms. A positive history of cutaneous lesions was not elicited from the parents. The patient's son, aged 49, did not have skin lesions but had arcus senilis. Her elder daughter was noticeably affected and the younger daughter had xanthoma palpebrarum. Familial tendency has been stated to be due to an irregular dominant without sex limitation.

Katz, S., Cake, C. P., and Reed, H. R. (1943) *New Engl. J. Med.*, **229**, 498.

Love, J. G. (1944) *Proc. Mayo Clin.*, **19**, 113.

Selye, H. (1943) *Arch. Derm. Syph., N.Y.*, **48**, 188.

Swanson, J. C. (1943) *Brit. J. Derm.*, **55**, 289.

Thomson, S. (1943) *Brit. J. Derm.*, **55**, 267.

SMALLPOX

See also B.E.M.P., Vol. XI, p. 269; Interim Supplement, No. 20*; and Cumulative Supplement, Key No. 1416.

Pathology, bacteriology, and morbid anatomy**Propagation tests**

Passage of two virus strains through rabbits' testes.—Experiments in the propagation by rabbit testicular passage of the variola virus have been carried out by Nelson. Two strains of virus were used in the work, (1) a strain obtained from China in 1940 and since maintained by 44 transfers in embryonated eggs and (2) a strain isolated in 1938 from a case of smallpox in Minnesota and similarly transferred 200 times. Neither virus showed any alteration in behaviour in the egg as the result of these passages. Egg membrane suspensions, shown to be bacteriologically sterile, were injected into one testis of normal rabbits, the dose being 0.5 cubic centimetre of a 10 per cent suspension. The rabbits were kept separately under strict quarantine. They were killed on from the third to the seventh day. The injected testis, after a small piece had been removed for histological study, was ground up, and suspensions of different strengths were made and used to inoculate embryonated eggs. It was found that the virus could be demonstrated in rabbits killed on the third day but not in those killed on the fifth day, nor in passaged rabbits. It was found, however, that in the latter case although a single egg transfer might fail to show the presence of variola virus, a second egg transfer gave the characteristic variola reaction. The Chinese virus was maintained for 11 rabbit passages without significant alteration. It proved to be impossible to maintain the Minnesota strain beyond the third testicular passage. No evidence of vaccinal transformation of either virus was obtained.

Clinical picture**Smallpox and tuberculosis**

Notes on four cases.—Keers and Steen report 4 cases in which vaccination against smallpox appeared to cause a latent tuberculous focus to flare up. (1) A man 28 years of age was vaccinated prior to acceptance for work abroad. He had a severe reaction and on the sixth day an acute left-sided pleurisy with effusion developed. Radiography revealed bilateral infiltration with cavitation in the left upper zone. He had previously felt perfectly well and had passed a medical examination for his new job. (2) A man aged 22 years had received sanatorium treatment and had been symptom free for 3 years. In his case pleural effusion developed with radiographical evidence of renewed activity after vaccination. (3) A man 20 years of age had had sanatorium treatment and had been without symptoms for a year. After vaccination a fresh area of disease and positive sputum developed. (4) A girl who was 19 years old developed signs of pulmonary tuberculosis with haemoptysis a few weeks after vaccination.

Treatment**Prophylactic**

Further proof of efficacy of vaccination.—The value of vaccination in the protection of a community from smallpox is once again demonstrated by Coleman's account of a case which occurred in a British Army unit in India. In one of the men, who had been vaccinated while in the Army 3 years before but who showed no mark of vaccination, fatal haemorrhagic smallpox developed. He had mixed with his companions in barracks for about 18 hours after he first felt ill, so that all 938 were regarded as contacts and were revaccinated. All had been vaccinated within 5 years. In 70 per cent a reaction occurred within 48 hours; in 22 per cent it was delayed for 96 hours. In all it was mild and faded rapidly. In none was a classical response observed. In 3 per cent a doubtful response was obtained and vaccination was repeated. Only 5 per cent of these gave the classical response. No further cases of smallpox occurred.

Coleman, P. N. (1944) *Brit. med. J.*, 1, 191.

Keers, R. Y., and Steen, P. (1943) *Brit. J. Tuberc.*, 37, 111.

Nelson, J. B. (1943) *J. exp. Med.*, 78, 231.

SPEECH DEFECTS

See also B.E.M.P., Vol. XI, p. 294.

Stuttering**Treatment**

Rumsey states that in all speech defects there is a loss of speech balance, and that to restore the balance should be the aim of the therapist. Speech defects are mostly found in people who have cleft palates or who stammer because of shyness or for some other nervous reason. It is comparatively easy to teach the stammerer how to control the stammer by speaking slowly, firmly, and smoothly. It is a well known fact that people with speech defects can sing with fluency because there is in the mind a picture of the tune and rhythm of the song. If stammerers could lose their anxiety about producing the speech, ease of voice production would follow automatically in most cases. The voice is produced in the larynx and the mouth forms the vowels and consonants, that is words. With stammerers the mouth does too much work and the larynx too little. In cases of cleft-palate speech the unpleasant nasal tone can be corrected by development of chest resonance, by exercises for the closure of the naso-pharynx and by

placing the voice forward to the front of the palate. In cleft palate the aim should be to increase audibility rather than to correct the apparent defect. This is done first by production of the voice from the larynx, then by clear enunciation of the vowels and lastly by correct articulation of the consonants.

Rumsey, H. St. J. (1944) *Med. Pr.*, **211**, 139.

SPINAL CORD DISEASES

See also B.E.M.P., Vol. XI, p. 302.

Tumours

Arachnoiditis or meningitis serosa circumscripta

Aetiological influence of thrombocytopenic purpura.—Nelson, dismissing syringomyelia as a developmental defect, discusses whether adhesive arachnoiditis causes or results from intramedullary cavitation. His patient, aged 50 years, had suffered from epistaxis and easy bruising until he was 26 years old. Recurrence of epistaxis with ecchymoses and convulsions at the age of 46 caused his admission to hospital where blood examination, showing delayed clotting and a platelet count of 20,000, prompted a diagnosis of thrombocytopenic purpura. The Wassermann reaction was negative. On readmission 3 years later myeloscopic examination at the level of the second lumbar vertebra revealed tautness of the dura mater and immobility of the spinal nerve roots such as would be caused if they were fixed by adhesions. To the former diagnosis of thrombocytopenic purpura, which was thought to be responsible for a haemorrhage in the right cerebral hemisphere which caused convulsions and left hemiparesis, was added that of arachnoiditis of the lumbar cord. Fifteen months later increased paralyses with urinary infection proved fatal. At necropsy the dura mater was found to be adherent to the cortex. The pia-arachnoid membranes were opalescent and were adherent around frontal lobes, optic nerves, temporal lobes, cerebellum and pons. Outside the internal capsule of the right hemisphere was an area of softening and discoloration. The lower dorsal cord showed numerous cavities and one large cavity hollowed the lumbar cord. A history of alcoholism and malnutrition probably had no bearing on the causation. Fibrotic organization after repeated meningeal bleeding was considered to have caused the cavitation.

Nelson, J. (1943) *Arch. Neurol. Psychiat.*, Chicago, **50**, 1.

SPINE, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. XI, p. 361.

Prolapse and calcification of intervertebral disks

Ruptured lumbar intervertebral disks

Advances in diagnosis and treatment.—Dandy states that the diagnosis and localization of ruptured lumbar intervertebral disks are almost absolutely certain, that they are now among the most common lesions to be treated by surgical procedure and that their cure is practically assured. In 95 per cent of cases of low backache and sciatica a ruptured disk is the cause. In 5 per cent the cause may be (1) spondylolisthesis (2 per cent); (2) congenitally defective fifth lumbar vertebra (2 per cent); (3) tumours of the cauda equina (1 per cent). In diagnosis X-ray examination is as important as is examination of the Achilles reflex. When the reflex is reduced or absent the affected disk is usually at the fifth lumbar vertebra. Special injections of lipiodol are unnecessary for diagnosis. There are two types of disks, (1) protruding and (2) concealed; the symptoms are the same in both types; the necrotic interior of the disk causes backache and the protruding part causes sciatica. At operation the exposure is unilateral and between the laminae without removal of bone except for a portion of lamina where the opening is small. The necrotic contents must be scraped away. Fusion of the vertebrae usually occurs after operation. Mobility of the vertebra will generally indicate whether the disk is at the fourth and fifth lumbar vertebrae (which it is in 98 per cent of cases) or at both. The high percentage is probably due to a shift in the plane of the articular processes from the horizontal to a transverse direction.

The protruded disk

Clinical characteristics and treatment.—Love and Walsh give an account of the clinical characteristics and treatment of protruded intervertebral disks. It is generally recognized that the lesion is caused by trauma but the predisposing factors are not clearly understood. In all cases the patient's history is one of the most important parts of the examination. Pain is the cardinal symptom and in severe cases may lead to the patient's loss of weight from insomnia and anorexia. In longstanding cases irreparable damage to the nervous system may occur. A competent orthopaedic examination is essential although neurological examination may by itself demonstrate sufficient positive findings to indicate an intraspinal space-taking lesion; a radiological examination should also be made. In all doubtful cases lumbar puncture should be performed and a careful analysis of the cerebrospinal fluid must be made. The diagnosis in classical cases is not difficult. There is loss of lumbar lordosis, marked spasm of the erector spinae muscles and limitation of spinal movements with tenderness over the spinous processes of the lowest lumbar vertebrae. Straight leg raising during recumbency is painful and limited on the side of the sciatic pain and in severe cases there may be bilaterally positive responses. The Achilles reflex on the affected side is generally diminished or absent. Neoplasm of the

spinal cord may simulate the condition and should be remembered in the differential diagnosis. When the diagnosis of protruded intervertebral disk is confirmed and operation is indicated, the latter should be performed without delay. The protruded fragments of the disk are removed; in the majority of cases the dura mater need not be opened and it is unnecessary to sacrifice any bone; in some cases laminectomy is required. The advisability of performing a bone graft at the time of removal is debatable but the authors suggest that a bone graft is sometimes necessary to produce the best results; a fusion operation, however, necessitates a much longer period of treatment in hospital. The results of operative removal of protruded intervertebral disks are excellent and in the authors' subjects the mortality rate is less than 0.25 per cent.

Dandy, W. E. (1943) *Ann. Surg.*, **118**, 639.

Love, J. G., and Walsh, M. N. (1943) *Surg. Gynec. Obstet.*, **77**, 497.

STERILITY

See also B.E.M.P., Vol. XI, p. 447; Interim Supplement, No. 19*; and Cumulative Supplement, Key Nos. 1455–1457.

General aspects

Causes of infertile marriage

Classification and treatment of infertility.—Deficiencies in the male account for nearly half the number of sterile marriages. Henry classifies deficiencies in the female as embryological, mechanical and functional. A maldeveloped Müllerian tract results in a rudimentary uterus with amenorrhoea or scanty menstruation although development of secondary sexual characteristics demonstrates some ovarian activity. Medication with oestrogen and progesterone sometimes produces bleeding but not true menstruation and offers little hope of pregnancy. Mechanical obstruction is usually tubal and of inflammatory origin. The infection is commonly gonococcal but non-specific infections after parturition and adhesions from pelvic inflammation which externally compress the tubes demand recognition. The passing of air through the tubes or the injection of lipiodol under pressure not exceeding 150 millimetres of mercury should be carried out between the twelfth and twenty-first days of the menstrual cycle in order to exclude results falsely negative. Surgical measures are unsatisfactory but heat applied by Elliott's vaginal bag promises some success. Functional sterility, abortion and habitual abortion are shown by 2 recently devised tests to arise from disordered function of the corpus luteum. In treatment of such cases, first, a fragment of endometrium is removed immediately before or after the onset of menstruation with a minute curette; the fragment may show changes which indicate progesterone deficiency or, rarely, it may show the effects of the oestrogenic hormone only and thus indicate that ovulation has not taken place. Secondly, assay of the progesterone which is excreted as pregnanediol during the 12 days after the end of the menstrual mid-cycle shows a normal condition if the amount excreted is from 35 to 60 milligrams whereas if the amount is less than 35 milligrams the condition is one of functional sterility. The two tests are exactly confirmatory and show all grades of abnormality. Some apparent progress after the administration of the luteinizing hormone found in the urine of pregnancy which stimulates progesterone secretion, suggests a line for future investigation.

General review.—In a report on an investigation of sterility Page and Page review their own cases and detail the methods they use in the diagnosis and treatment of the condition. Spermatozoa should exceed fifty million per cubic centimetre and 70 per cent should be motile 2 hours after ejaculation. Persisting motility and, in the stained smear, less than 20 per cent of heteromorphous spermatozoa show that the husband is probably not responsible for the sterility. If faulty spermatogenesis is detected physical examination is necessary. Endocrine or dietary deficiencies indicate that thyroid extract should be administered, that a high protein diet and large doses of vitamin B complex should be taken, that sexual activity should be reduced and relaxation and sleep increased. The time relationship of fertile coitus and ovulation should be explained to the couple, who should also be advised to discontinue the use of (possibly spermicidal) lubricants. In the authors' cases the female aspect of the problem was studied at 3 consultations. First a complete gynaecological and general history was taken. A chart was provided for recording the menstrual cycle, dates of coitus and the morning vaginal temperature the curve of which, as described by Rubenstein, has in the authors' opinion superseded biopsy as an index of ovulation. The patient also charted the pulse rate to serve as a guide in possible thyroid administration. The second consultation covered examination of laboratory reports, gynaecological examination and tubal insufflation; the last was repeated if necessary at the third consultation when the post-coital study was made. The data acquired by these means will suggest vaginal, cervical, uterine, or systemic treatment. The cure of vaginitis, especially that of trichomonas origin, and of hyperacidity will often promote conception. Uterine malpositions should be corrected by the use of a pessary, erosions should be treated and unsatisfactory findings from the post-coital study may indicate that electrocoagulation of the canal should be done. Fibroids must be removed. An endometrium unprepared for nidation may benefit from premenstrual administration of progesterone but hormone therapy generally is of little avail. Tubal occlusion may require repeated insufflations; in the series under review this treatment was successful in 50 per cent of cases. Defective ovogenesis may

indicate hypothyroidism or that there is a systemic disease. Of 180 female patients seen by the authors 18 were incurably sterile. The cooperation of 60 was incomplete, yet 12 conceived. Of 102 who persevered with treatment, 48 became pregnant.

Sterility in the female

Causes

Management of the sterile patient.—Bourne is chiefly concerned here with the female partner in an infertile marriage and considers the significant points in history-taking. If coitus takes place too often the male is rendered subfertile; if too seldom it may fail to coincide with ovulation. Although it is not essential to fertilization the experience of orgasm by the female is a useful biological event since it provides a mucous path by which the spermatozoa may reach the uterus. Late puberty, infrequent menstruation during adolescence, initial dysmenorrhoea and unequal menstrual cycles suggest that the reproductive organs are hypoplastic. A history of suppurative appendicitis or pyrexia after miscarriage suggests the presence of pelvic adhesions. Obvious obesity or symptoms volunteered by the patient may indicate the presence of hypothyroidism. Examination should be made about 2 weeks before the start of the next period. Fibroids may be palpated through the abdominal wall, vaginal hyperacidity lethal to spermatozoa be detected and orificial obstruction, organic or functional, be discovered. If examination by speculum shows a mucosa thin, red and smooth instead of pink and rugose, it is probable that oestrus and ovulation are absent. Abnormal cervical secretions and pus which suggests trichomonas infection can be noted. Bimanual examination will detect an undersized uterus or tubal swelling. Insufflation of the utero-tubal passage will test the tubal patency. A fragment removed by the biopsy curette during the pre-menstrual week which displays the secretory phase of the mucosa is not conclusive of ovulation. An isolated specimen is valueless and monthly repetition throughout a year would be necessary in order to assess ovulation with any reasonable accuracy. Salpingography, after injection of the uterus with lipiodol, will confirm—or sometimes contradict—the findings of insufflation, will localize obstruction and may prove to be curative. In treatment, dilatation overcomes minor orificial obstruction. Major obstruction yields to surgery but vaginismus should be referred to the psychotherapist. The cure of vaginitis makes conception more likely. Cervical infections require treatment by cauterization. A douche of sodium bicarbonate, one teaspoonful to the pint, given 2 hours before coitus, neutralizes hyperacidity. Before the age of 25 years an undeveloped uterus may be stimulated by administration of the pituitary gonadotrophic hormones or by giving stilboestrol after, and a corpus luteum extract before, a period. Prolan A (the follicle-stimulating hormone), which is successful in the laboratory has failed clinically to stimulate ovulation. In tubal occlusion whereas repeated insufflation often succeeds, surgery fails. In cases in which hypothyroidism is responsible for the sterility, prognosis is hopeful. When both husband and wife appear to be normal not any of the methods of treatment at present known appears to be effective in overcoming sterility.

Treatment

Artificial insemination.—Guttmacher reviews the present knowledge and history of artificial insemination in the treatment of human sterility; he points out the limitations of as well as the indications for this much applauded cure. Historically, artificial insemination is one of the rare medical entities which cannot be traced back to Hippocrates; the first human application was made only a century and a half ago. The earliest references given by the author are to an Arabian Sheik anxious to improve his horseflesh and to Swannerden of Leyden in 1680 and Abbe Lazzaro Spallanzaani (1729-99); in 1799 Hunter is quoted as interested in the case of a man anxious to undergo the procedure. The author mentions Sims and during the last 30 years Engelman, Schorokoka, Cary and Seymour and Koerner as writing on the subject. A remarkable item in Seymour and Koerner's paper is that more than 97 per cent of all the pregnancies due to artificial insemination terminated normally. Indications for artificial insemination are to be found in (1) cases in which intravaginal coitus between two fertile individuals is impossible because of mechanical factors; (2) an inclusive group of sterile individuals; (3) cases in which the husband is sterile and the wife apparently sterile. It is stated that most practitioners accept cases in groups (1) and (3). The author has formulated the following moral and legal problems. Rule (1) The donor must remain completely anonymous to the recipient and to her husband and the recipient and the husband must remain equally anonymous to the donor. Rule (2) There must be knowledge of the couple, their intellectual capacity and emotional stability and if possible the likelihood of a permanent marriage. Only a small percentage of patients applying qualify for so radical a procedure. When a doctor consents to do an artificial insemination from an unrelated donor it is really the couple's insignia of good character. Rule (3) The procedure must never be urged; if either husband or wife are not wholly in favour of it, the idea must be completely given up. Rule (4) Forget signed papers. If the patients are selected carefully, contracts and agreements are unnecessary and simply act as a permanent reminder of something which should be forgotten as quickly and as completely as possible. Rule (5) Accord paternity to the husband both in the hospital record and in the birth certificate. Rule (6) Make the fees low; keep artificial insemination out of the mercenary column. Artificial insemination received little attention until veterinary surgeons showed human practitioners its great possibilities. Wanoff, the Russian pioneer, is specially mentioned in this connexion.

Sterility in the male**Causes**

Low fecundity in the male.—A recent Report on sterility and impaired fertility embodies the conclusions reached at a conference convened by the British Social Hygiene Council. It is estimated that about one-tenth of the number of all British and American marriages remain childless. That permanent childlessness is rarely deliberate is indicated by the findings of two independent investigators who questioned groups of childless wives; they affirmed that in about 90 per cent of childless couples who had been married for 5 or more years and in about 60 per cent of couples with one child only the lack of offspring was the result not of choice but of low reproductive capacity. Data collected by individual clinicians and clinics show that in only about 5 per cent of young couples is birth control used with intent to procure permanent childlessness. Among the working classes contraceptive assistance is rarely sought by women who have not had at least one child. Thus in one group of over 200 women who regularly practised birth control the average number of children was greater than in a control group of women using similar methods intermittently. Investigations show also that the contraceptive methods most commonly used by working-class people are notoriously unreliable and that their seeming success can be shown to reflect impaired fertility in at least one-third of the number of cases. In a series of 100 childless couples in which the husband's semen had been examined the following findings were noted. (1) No apparent abnormality in either partner 20 per cent. (2) Abnormalities in the wife: blocked or rigid uterine tubes 41 per cent, obvious endocrine defects 7 per cent. (3) Abnormalities in the husband: azoospermia 11 per cent, impaired fertility 43 per cent. Low fecundity in the male appeared to be common; examination of about 100 volunteers revealed impaired fertility in at least 20 per cent.

Surgical treatment

Epididymovasostomy as a cure.—An unusual case of sterility reported by Marquardt and Baumann was observed in one of 55 men examined for sterility. The patient, aged 34 years, had been married for 5 years. He gave a history of a severe attack of double gonorrhoeal epididymitis 4 years before marriage. Physical examination, otherwise negative, revealed a nodule of induration in the lower pole of each epididymis. Specimens of seminal fluid were examined on 3 occasions and were shown not to contain any spermatozoa. Aspiration of the epididymis was carried out on both sides and live spermatozoa were obtained from the left. Epididymovasostomy was suggested but was declined by the patient. Two years later, having changed his mind, he underwent the bilateral operation. Three months afterwards the ejaculate contained 85 million spermatozoa and within 4 months the patient's wife conceived. The authors have failed to discover any other case of sterility of this duration cured by epididymovasostomy.

Bourne, A. (1944) *Practitioner*, **152**, 135.

Guttmacher, A. F. (1943) *Bull. N.Y. Acad. Med.*, **19**, 573.

Henry, J. S. (1943) *Canad. med. Ass. J.*, **49**, 167.

Marquardt, C. R., and Baumann, A. J. (1943) *Urol. cutan. Rev.*, **47**, 502.

Page, E. W., and Page, C. W. (1944) *Urol. cutan. Rev.*, **48**, 11.

Report (1943) *Lancet*, **2**, 457.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

See also B.E.M.P., Vol. XI, p. 476; and Cumulative Supplement, Key Nos. 1461–1464.

Malignant tumours of the stomach**Course and prognosis**

Carcinoma of the stomach.—Dochat and Gray have studied two of the factors which influence the prognosis in carcinoma of the stomach. In 1936 the disease accounted for 22 per cent of all deaths from cancer for that year. In 1941 operation was attempted in only 33.3 per cent of cases seen at the Charity Hospital, New Orleans, and the mortality rate was 50 per cent for gastrectomy operations; only one patient in every 30 with the disease left the hospital alive and only about one-third of the number of such patients survived for 5 years after operation. The chances of cure therefore appear to depend largely upon early diagnosis. A series of cases has been analysed and the authors consider that the grade of malignancy (Broders's classification) and the extent or spread of the lesions are two factors of great prognostic significance. In 1932 Dukes evolved another system of classification which he used in conjunction with Broders's method for 215 cases of carcinoma of the rectum. In the present study both Dukes's and Broders's systems were used in an attempt to type gastric carcinomas for the estimation of survival time in individual cases. A series of 1,251 cases was investigated comprising all the operative cases of gastric carcinoma seen at the Mayo Clinic from 1922 to 1934. Histological examinations were made in all cases. The carcinomas were divided into 4 grades according to the extent of the lesion. The prognosis appears to be excellent in cases which belong to the two lower grades, but the chance for post-operative survival is poor if they belong to either of the others. The authors consider that the combined methods of classification, by grade of lesion and extent of spread, afford a valuable guide to prognosis but that either method employed separately is inadequate for the purpose of assessing the possible survival time.

Dochat, G. R., and Gray, H. K. (1943) *Amer. J. clin. Path.*, **13**, 441.

STRABISMUS

See also B.E.M.P., Vol. XI, p. 492; and Cumulative Supplement, Key No. 1465.

Paralytic squint*Treatment*

Selection of suitable muscles for operation.—Sugar considers the question of the amount of operative correction and the selection of proper muscles for operation in various types of squint. The results of 65 operations on the internal and external recti muscles of men in the United States Army, aged from 20 to 49 years, are analysed. Only 2 types of operation were performed, namely (1) recession and (2) resection and only cases of convergent and divergent squint with no vertical component and of the non-accommodative type were selected. The maximum amount of muscle resected was 7 millimetres; this was also the greatest amount of recession performed. Fairly consistent results were obtained. Resection of the internal rectus resulted in greater correction than did recession of that muscle, whereas the opposite result was obtained by operation on the external rectus. Combined resection and recession resulted in approximately the same amount of correction for all varieties of squint selected. One most interesting result was that with an equal resection and recession of 7 millimetres each, the amount of correction obtained was approximately twice that obtained with an equal resection and recession of 5 millimetres each. This is considered to be related to the subsidiary duction action of the superior and inferior rectus muscles. No difference in the amount of correction obtained was found when the operation was performed on the deviating or fixing eye in cases of monocular squint. The author considers that the relative near point of convergence is the deciding factor in choosing which type of operation should be performed. This refers only to the smaller degrees of squint since in the majority of cases of large deviations the measurements for distance and near vision are the same. In the latter cases, up to 7 millimetres of correction in each of the rectus muscles of the deviating eye was performed and the correction for the residual deviation was divided between the horizontal muscles of the other eye.

Orthoptic treatment.—Pugh observes that although squint may be present at birth, most squints occur between the ages of 2 and 5 years whereas in a much smaller number of children they develop between the ages of 5 and 10 years. Fifty per cent of squints have as an aetiological basis an error of refraction. Psychological traumas, of which jealousy is probably the commonest, account for between 10 and 20 per cent of cases. The so-called familial tendency is explained by the imitative faculty of the child. The cause of the remaining 30 per cent of cases may be the disproportionate strength of one or other of the ocular muscles. Orthoptic training aims to establish two eyes which will maintain a normal position at any required focus and with full visual acuity in each. The first stage is concerned with the development of the visual acuity of the weaker eye and this should be initiated as early as possible. If the weak eye does not fix centrally when the other is covered the difference of acuity between the eyes is marked. The application of an adhesive patch which completely covers the stronger eye is the most satisfactory measure. The vision of each eye should be checked every month as in young children the covered eye can become amblyopic. When the vision has developed to 6/12 the patch is replaced by an occluder attached to the spectacles. The results in patients over 8 years of age are disappointing because a good result is then exceptional; the optimum age is about 7 years. Exercises for the purpose of developing normal binocular vision are begun on an amblyoscope as soon as the vision in the weaker eye is 6/18 and as soon as the patient will cooperate. The number of patients who recover normality by orthoptic training alone is disappointingly low—10 to 15 per cent. Surgery alone gives only a 50 per cent rate of success, and the number of operations which succeed in putting the eye in the exact necessary anatomical position is less than 10 per cent. The combined methods of spectacles, occlusion, orthoptic training, and surgery if necessary, give between 80 and 90 per cent of successful results. Heterophoria responds to general measures taken for the purpose of improving the patients' health and to orthoptic treatment. Conditions of paralytic squint secondary to trauma and to sinus disease are helped by exercises.

Comitant (concomitant) or non-paralytic squint*Treatment*

Orthoptic methods.—Walraven maintains that the most important factor in the orthoptic training necessary to develop binocular vision in cases of strabismus is the intelligent and persevering cooperation of the child's parents. This can usually be obtained by giving parents at the outset a very thorough explanation of the reasons for and the object and advantages of orthoptics and by laying particular emphasis on the length of time needed for success in most cases. A warning about the possible additional necessity of surgical intervention or of the wearing of glasses should also be added. In cases of amblyopia complete and constant occlusion of the fixating eye for a period of time, which depends upon the age of the child and the length of time that squint has been present, is imperative. Almost invariably such treatment is readily accepted by the child provided the parents adopt a sensible attitude towards it. A gauze pad held in place with adhesive tape, the eyebrow and eyelashes being first smeared with vaseline, will cover the eye effectively. Patients without fusion, with abnormal retinal correspondence and with large deviations must commence their training under expert supervision but for the most part orthoptic exercises are of necessity carried out at home.

The adoption of a planned and regular daily routine under the sympathetic guidance and with the active participation of the parent is most helpful in developing the child's perseverance and in stimulating the mental effort he is required to make in performing the exercises correctly. The importance of good general health, balanced diets, outdoor exercise and rest should not be overlooked.

Roth describes orthoptic methods in diagnosis appropriate to children under from 1 to 4 years old. Cases of pseudostrabismus due to a wide epicanthus are dismissed by the ophthalmologist after he has reassured the parent; for hypermetropia exceeding +8 diopters he prescribes glasses, which even babies will not refuse to wear. In cases of organic strabismus the orthoptist in several sittings investigates visual acuity, fixation, angle of deviation and fusion. To estimate vision the kindergarten and Berens charts, the Landolt broken ring or graded blocks are employed as in a game. The fixating eye in monocular squint, or the preferred eye in alternating squint, is determined. If future occlusion is necessary in order to prevent amblyopia ex anopsia or secondary contractures, the reason for and method of occluding the better eye are explained to the parent. The angle of squint is measured by cover tests after the age of 3 years or by the Hirschberg method for infants. Monocular and binocular rotations are attempted. Binocular vision is next investigated by the use of Worth's dot test when possible, otherwise of coloured toys. The measurement of squint and retinal correspondence on the major amblyoscope is the next aim; a quick flash is made when the patient is absorbed in the 'lion and cage' or 'spider and web'. Repeated corroboration of findings is essential. Since distaste for orthoptic exercises readily arises and much concentration is needed, regular treatment is postponed to the appropriate age.

Pugh, Mary (1944) *Practitioner*, 152, 88.

Roth, Edith V. (1944) *Amer. J. Ophthalm.*, 27, 57.

Sugar, H. S. (1943) *Arch. Ophthalm.*, N.Y., 30, 593.

Walraven, Frances (1943) *Amer. J. Ophthalm.*, 26, 1175.

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

See also B.E.M.P., Vol. XI, p. 503.

Clinical applications

General

Review of diseases of sympathetic system.—Bing reviews what is known of the symptomatology, pathogenesis and treatment of the diseases of the sympathetic system comprised under the heads of (1) herpes zoster, (2) erythromelalgia, (3) erythropsopalgia, (4) causalgia and (5) Raynaud's disease. (1) He points out that in herpes zoster the presence of the skin eruption indicates that not only the sensory fibres of the posterior roots are involved but also the non-medullated vegetative fibres which have been shown by numerous workers to pass in both directions through the posterior roots. Suspension of the normal histotrophic function of these fibres may be supposed to underlie, in some way not yet understood, the changes in the skin which result in the formation of vesicles. (2) In erythromelalgia the causative lesion appears to be situated in the peripheral nerves. The precipitating cause may be cold, immersion, infection or strain but in addition a constitutional inferiority of the sympathetic nervous system must be supposed to exist. Many of the patients also have migraine, asthma or some other sympathetic affection. (3) A similar syndrome occurring in the face has been described by Bing as erythropsopalgia. The symptoms consist in attacks of pain, redness and swelling of one or both sides of the face with profuse rhinorrhoea. (4) In causalgia the peculiarly affective character of the pain seems to indicate that it originates in the sympathetic system and is in fact a sympathetic neuralgia. (5) In Raynaud's disease causalgic pain is absent and the condition can be described as a trophic and vasomotor neurosis. Only in the last-named affection can periarterial sympathectomy be expected to give good results. In the other sympathetic affections it nearly always proves to be useless if not harmful, and they are best treated medically with the ordinary analgesics, the action of which is often enhanced by the addition of scopolamine. Opiates should be avoided because of the risk of habituation.

Bing, R. (1944) *Schweiz. med. Wschr.*, 74, 275.

SYPHILIS

See also B.E.M.P., Vol. XI, p. 526; and Cumulative Supplement, Key No. 1467.

Congenital syphilis

Treatment

Serological tests.—Wattie considers that to combat promiscuity by the education of young people is the first step in overcoming congenital syphilis; the second step is the provision of antenatal care for all pregnant women and the third is the identification of those venereally infected. Antenatal care by specialists in organized clinics makes foetal infection preventable. The integration of the antenatal and child welfare clinic and the maternity hospital is essential. Unobtrusive treatment must be provided in the place in which the diagnosis is made. Segregation in venereal clinics is detrimental. A serological test should be performed at the first attendance and confirmed if found positive. Maternal syphilis of more than 5 years' standing

rarely infects the foetus but a strongly positive reaction is always an indication for treatment. The diagnosis of less established syphilis is difficult since pregnancy ameliorates and masks the disease. Only a strongly positive Wassermann or Kahn test is reliable. If early manifestations are present in the mother, especially when infection is acquired in advanced pregnancy, the prospect of her bearing a healthy child is poor. During 1943, of 17 children whose mothers showed primary or secondary manifestations during late pregnancy, 4 died within 3 months of birth, despite treatment. Nine children however, although serologically positive, did not exhibit clinical manifestations; this fact illustrates the value of even brief maternal treatment. Three serological tests at intervals throughout pregnancy are an ideal, but the expenditure of time and material which would be necessary are not justified, since an infection which fails to produce pain and discomfort rarely occurs after the initial test. The potentially syphilitic infant, however, requires a test at the first, third and twelfth month as a false negative often occurs up to the third month. Since antenatal treatment was instituted in Glasgow in 1924, a notable fall from 202 cases of congenital syphilis in that year to 39 cases in 1939 and 15 cases in 1941 occurred. The ordinary marital infection has been controlled. War conditions have introduced a number of cases of acute infection acquired during pregnancy, with a consequent increase in congenital syphilis. This new problem can be solved only by the notification of venereal diseases.

Treatment

Arsenical compounds

Mapharsen by intravenous drip.—Craig and Sadusk report 3 years of trial of massive doses of mapharsen (mapharside) by means of a 5-day continuous intravenous drip for early syphilis, as administered in 74 cases. The cardinal points to be observed are, (1) establishment of the diagnosis of early syphilis; (2) exclusion of patients with fever, liver disease or severe nephritis; (3) periodical re-examination in order to determine whether or not further treatment is necessary on the basis of the serological reaction 6 months later or of a relapse. Every patient receives a total dose of arsenic which has been found to be sufficient for cure in four-fifths of the number of those treated; whereas patients who receive the usual weekly injections do not as a rule complete an adequate course of treatment, these in-patients complete their treatment before discharge. When the patient leaves hospital after massive therapy he is not infectious and remains so in nearly every case. The disadvantage is the danger of an occasional severe toxic reaction, which rarely may be fatal. The toxic reactions encountered were primary fever (Herxheimer reaction) 27 times in 74 patients, secondary fever in 24 patients, drug rashes in 17, local venous thromboses in 24, secondary anaemia in 17 and peripheral neuritis in 30. There was vomiting in many cases. Severe peripheral neuritis with temporary paralysis and also jaundice occurred in one patient. The actual administration of the drug is relatively simple. Solutions were made up twice daily—1,200 cubic centimetres of 5 per cent glucose in a Fenwall flask with 120 milligrams of mapharsen. A strip of adhesive plaster on the side of the flask was marked with the levels at which the fluid in the flask should stand at various hours. Rate of flow was regulated with reference to the marks. The contents of 2 flasks (2,400 cubic centimetres containing 240 milligrams of mapharsen) were given daily over a period of 12 hours for 5 days which makes a total for each patient of 1·2 grammes. Satisfactory results were obtained in 79 per cent of patients as observed after 6 months or more. Selected cases were re-treated, and the total of satisfactory results was thus raised to 87 per cent. Of the remaining 13 per cent, some have not been watched for long enough after re-treatment to ascertain the final result. Except for a positive spinal fluid reaction in one case, the only evidence of syphilis in these patients was the positive serological reaction.

Phenarsine.—In treating 112 cases of syphilis with phenarsine hydrochloride (a mechanical mixture of 3-amino-4-hydroxy-phenyl-dichlorarsine hydrochloride), or clorarsen, Boardman and Kaldeck employed doses ranging from 0·03 gramme to 0·05 gramme for women and to 0·067 gramme for men. From 10 to 20 injections constituted a course. Cases of early syphilis received 3 injections weekly for 2 or 3 weeks and thereafter one injection weekly. In later courses injections were given weekly throughout. Fifteen injections of bismuth were given after each phenarsine course, the weekly injection containing 0·075 gramme of bismuth subsalicylate in 1 cubic centimetre of peanut oil. In late syphilis a bismuth course was given before administration of phenarsine. Pregnant women received phenarsine only. Transference to more adjacent clinics and other circumstances during the period under review reduced the number under treatment to 47. Reactions, mostly gastro-intestinal, developed in 25 patients but the giving of phenarsine was discontinued in 7 cases only, including one patient with jaundice and anaemia who recovered on administration of bismuth, and one with dermatitis. The average time for disappearance of primary and secondary lesions was 22 days. Of 7 cases of primary syphilis 6 attained serological negativity in an average time of 11 weeks; of 7 secondary cases 6 averaged 15 weeks; of 33 cases of late syphilis 3 attained negativity in 33 weeks. Equality in success of treatment with phenarsine when compared with treatment with other arsenicals, and its low toxicity, warrant further trial of this drug.

Pyretotherapy

Additional to the use of antisiphilitic chemical agents.—Lowe gives an account of the history and of the results of treatment of syphilis by artificial induction of fever. In 1932 it was demonstrated that the thermal death point *in vitro* of *Treponema pallidum* is 42° C. (107·6° F.) maintained for 1 hour or 40° C. (104° F.) maintained for 5 hours. Inability to raise the

temperature of all the tissues of the body to the thermal death point of *T. pallidum* probably accounts for the failure of artificial fever alone to cure early syphilis. The earlier in the course of the disease that such treatment is instituted the more favourable are the results. Huntley has obtained very good results from chemotherapy used in conjunction with artificial fever and noted a remission rate of 83 per cent and a clinical and serological improvement rate of 100 per cent. Ewalt and Ebaugh reported remission or improvement in 69 per cent of patients treated by artificial fever as compared with 58 per cent of patients treated by malaria. They also pointed out that patients with physical contra-indications to malarial therapy could be treated safely in many instances with artificial fever; the induction of malaria has therefore been discontinued by them. Bennett and his colleagues obtained good results from the use of chemotherapy when it was combined with artificial fever in the treatment of neurosyphilis. Simpson, Kendell and Rose noted that fever therapy conferred protection against anaphylactic manifestations in patients sensitive to arsenical compounds. They also treated a group of patients by a single intensive session of combined fever and chemotherapy using a preliminary injection of bismuth salicylate 4 grains and from 120 to 240 milligrams of mapharsen (mapharside) which was given by continuous drip transfusion. It appears evident (1) that artificial fever therapy fortifies and intensifies the action of antisyphilitic chemical agents, (2) that complications are minimized, (3) that neurosyphilitic patients can be treated as ambulatory cases and (4) that there is the possibility of obtaining cure by a single treatment.

Penicillin

Report on 4 cases.—Limited animal experiments have indicated that penicillin possesses some spirochaetocidal activity and that the time-dosage ratio will probably prove as important in the case of this drug as it does with other chemotherapeutic agents. Mahoney, Arnold and Harris treated 4 patients with early primary syphilis with penicillin only. Each patient displayed a single penile ulceration the diagnosis of which was established by dark-field examination. Each received an injection of 25,000 units of penicillin into the gluteal muscles every 4 hours, night and day, for 8 days. Dark-field studies, also made at 4-hourly intervals, failed to reveal any spiral forms in the secretions from the primary sore after the sixteenth hour. Mild but distinct clinical manifestations such as general malaise, pyrexia and headache were observed during the first 8 hours of treatment and the penile lesions became painful, with tenderness and swelling in the regional lymph glands. There was not however at any time any evidence to suggest toxic reaction to the drug, neither did the gluteal region show any irritative sequelae. Comprehensive routine sero-diagnostic tests were made throughout in order to determine the response to therapy. These indicated that the treatment was responsible for a comparatively rapid and complete disappearance from the blood stream of the reacting substance usually associated with activity in early syphilis. Further observation of the patients is to be maintained for as long as possible in order to note any evidence of relapse. Although their observations of results were recorded over a period sufficiently long to permit of comparison with the more conventional forms of treatment, the authors emphasize the fact that much study of many more cases over longer periods is necessary before any attempt is made to replace the present method of therapy by one based on penicillin.

Boardman, W. P., and Kaldeck, R. (1944) *New Engl. J. Med.*, **230**, 12.

Craige, B., and Sadusk, F. J. (1944) *New Engl. J. Med.*, **230**, 314.

Lowe, F. A. (1943) *Arch. phys. Ther.*, **24**, 587.

Mahoney, J. F., Arnold, R. C., and Harris, A. (1943) *Vener. Dis. Inform.*, **24**, 355.

Wattie, Nora I. (1944) *Brit. J. vener. Dis.*, **20**, 61.

TESTIS AND CORD DISEASES

See also B.E.M.P., Vol. XI, p. 656.

Tumours

Aetiology

Chorioma testis and sex-reversal.—Chorionic tissue in the testis, constituting chorioma testis, is classified as teratomatous, the reputed basis of teratoma formation being parthenogenesis. With this explanation Petillo is dissatisfied since atretic follicles, the seat of parthenogenesis, do not exist in the testis and to substitute the primordial germ cells is an evasion. Moreover, parthenogenesis is an asexual cleavage of the ovum which reproduces a specimen of the organism from which it derives. This orderly process would not produce a teratoma in which by Ewing's definition 'there is a notable lack of orderly arrangement' and a '*pot-pourri* of foetal tissue' is produced. The known phenomenon of sex-reversal is therefore adduced to explain why some 150 instances of chorioma testis are reported, in contrast with a dozen of chorioma ovarii, and also to explain the different age incidence in the two sexes. From this dozen are deducted 5 adult cases, as possible examples of ovarian pregnancy or of other conditions, leaving 7 instances confined to girls under 13 years of age. The author puts forward the following hypotheses. (1) The chromosome factor determining sex is liable to disturbances, thermal, chemical and traumatic, whereby a cell of one sex is transformed to the opposite sex. To such disturbances the testicle is more exposed than is the ovary, hence the preponderance of chorioma testis over chorioma ovarii; (2) the oogonia are far advanced towards maturity before puberty, hence reversal occurs in girls only during the first decade.

Auto-fertilization—the collision and fusion of sex-reversed spermatozoa or ova with normal spermatozoa or ova—is the explanation propounded. The embryo thus formed dies and degenerates and chorionic tissue persists.

Petillo, D. (1944) *Urol. cutan. Rev.*, **48**, 53.

TETANUS

See also B.E.M.P., Vol. XII, p. 1; Interim Supplement, No. 15*; and Cumulative Supplement, Key No. 1481.

Aetiology

Trauma

Suspected infection from instruments.—Eight cases of post-operative tetanus are reported by Bunch and Quattlebaum. (1) Three occurred in women in a 60-bed hospital for negroes. Each of the 3 had had a supravaginal hysterectomy. The first, aged 23 years, was operated on for tube-ovarian abscess and the adnexa and appendix were also removed; 6 days after operation she complained of stiffness of the jaws and inability to open the mouth. Convulsions and opisthotonos set in soon afterwards. Death occurred 2 days later. The second patient, aged 25 years, had a similar operation; trismus developed 6 days later, followed by convulsions, and she died on the ninth day after operation. The third patient, aged 40 years, had bilateral pyosalpinx and multiple fibroids. The adnexa and appendix were removed. Six days later trismus developed, this being followed by convulsions and opisthotonos. Death took place 8 days after operation. (2) The fourth case occurred in a hospital of 100 beds; a white woman aged 22 years had had a pylolithotomy and 17 days later she became affected by trismus and convulsions. She recovered after receiving 1,400,000 units of antitoxin. (3) Three cases occurred in another hospital. The first patient, aged 43 years, had a complete hysterectomy with removal of both tubes, one ovary and the appendix. The second, aged 38 years, had a subtotal hysterectomy for fibroids, with removal of both tubes and the appendix. In both patients tetanus developed on the fifth day and death took place on the sixth day. The third patient, a man of 38 years, showed signs of tetanus 7 days after amputation of the thigh and died the next day. (4) The last case occurred in a poorly equipped negro hospital in a woman who had a subtotal hysterectomy and appendicectomy. Tetanus developed on the fifth day and the patient died on the eighth day. In every one of these 8 cases instruments were sterilized by boiling. In no case was the diagnosis confirmed bacteriologically, owing to lack of laboratory facilities. The authors emphasize the dangers of imperfect sterilization and suggest that if the methods used cannot be relied on, prophylactic antitoxin should be given after every operation.

Immunity and immunization

Acquired immunity

Anaphylactic reaction to injection of tetanus toxoid.—Edwards points out that the prevalence of severe reactions after prophylactic immunization to tetanus has not been emphasized sufficiently in the literature and cites a case of anaphylactic reaction. In this subject, a man aged 29 years, 2 previous doses given at 3-week intervals had not caused any symptoms but after the third injection oedema of the eyes and lips occurred and subsequent collapse; the patient was unconscious for 20 minutes, was treated with epinephrine (adrenaline) hydrochloride injections and recovered; later he complained of intermittent epigastric pains the cause of which was not clear. There was not a previous history of asthma or of hay fever. Allergy studies in the form of skin tests and passive transfer reactions which were carried out later showed that the veal infusion contained in the toxoid was probably the factor which caused the anaphylactic reaction. The case demonstrates that severe reactions do occur even in patients without any history of obvious allergy. It is suggested by some workers that all patients who are to receive injections of tetanus toxoid should first be tested for sensitivity of the skin. Reference is made briefly to another case in which sensitivity tests had not previously been made and in which the young patient died 20 minutes after the injection of a second dose of plain tetanus toxoid which was combined with a third dose of typhoid vaccine. Artificial respiration and adrenaline injections were ineffective and post-mortem examination showed the presence of pulmonary oedema.

Treatment

Prophylactic

Comparison of toxoids used.—Alum precipitated tetanus toxoid is the more potent prophylactic of the two used in the treatment of tetanus but Miller and Humber commend fluid toxoid for stimulant injection after trauma as speedier in antitoxin production. They say also, in the immunization of children especially, that 3 injections of alum precipitated toxoid are to be preferred to 2. Each member of two groups of children comparable in age received 2 injections of 1 cubic centimetre of alum precipitated toxoid, the interval between the two injections being more than 8 weeks. Sixteen weeks later those in group (1) received 0.5 cubic centimetre as a third injection. Four weeks later both groups displayed at least 0.1 unit of antitoxin per cubic centimetre of blood. Of 39 children in group (1) one only displayed less than 1 unit. Of 46 in group (2) 20 displayed less than 1 unit. Thereafter the antitoxin level dropped more rapidly in group (2), so that between 3 and 6 months after immunization only

3 of 28 children in group (2) maintained 1 unit or over, whereas of 26 in group (1) 13 maintained this level. Between 9 and 15 months after immunization 9.5 per cent only of group (1) as against 27.7 per cent of group (2) failed to maintain 0.1 unit, the probable protective level. Although 3 injections best attain the paediatrists' aim of a year's immunity, renewable annually, the military ideal is a basic immunity attainable by 2 injections of alum precipitated toxoid reanimated in the wounded by a stimulant injection, for which the speedier fluid toxoid is here advocated, since tetanus may develop in a period of 5 days. Fifteen months after the end of the course described members of two groups of comparable titre were re-injected, those in group (a) receiving 1 cubic centimetre of fluid toxoid and group (b) 0.5 cubic centimetre of alum precipitated toxoid. On the fourth and fifth day a tenfold increase in antitoxin titre developed in 15 or 16 children in group (a) whereas a fivefold increase developed in 13 of 24 in group (b); at 7 days the increase was one hundredfold in group (a) and fortyfold in group (b).

Reinforcing protective dosage

Norman, reporting a case diagnosed as tetanus in an immunized subject, emphasizes the value of the procedure recommended in the Army of giving reinforcing doses of protective toxoid at yearly intervals to patients who have incurred the risk of tetanus infection. In these days tetanus seldom follows an obvious wound; it is more likely to occur after injuries so trivial that medical attention is not sought and prophylactic serum is not given. Norman's patient was a soldier, aged 27 years, who was admitted to hospital complaining of increasing pain and stiffness of the back. Two weeks previously he had had some septic sores on his legs. He had received 2 injections of tetanus toxoid 2 years before, on joining the Army. On admission symptoms of tetanus were noted. No bacteriological examination appears to have been made. The man recovered after receiving one dose of 200,000 units of antitetanic serum intravenously.

Bunch, G. H., and Quattlebaum, J. (1943) *Amer. J. Surg.*, N.S., **61**, 280.

Edwards, W. M. (1943) *J. Allergy*, **14**, 552.

Miller, J. J., Jun., and Humber, J. B. (1943) *J. Pediat.*, **23**, 516.

Norman, H. B. (1943) *Lancet*, **1**, 557.

THYMUS GLAND DISEASES

See also B.E.M.P., Vol. XII, p. 23; and Cumulative Supplement, Key No. 1483.

Diseases of the thymus gland

Myasthenia gravis

Epithelial metaplasia in thymic tumours.—Homburger records the changes in the thymus gland which occurred in all cases of thymus persistence or of tumour observed in a series of 6,000 necropsies and discusses the significance of such findings with especial reference to myasthenia gravis. In the author's series there were 14 cases of thymic enlargement in adults, 2 of which were cases of non-malignant thymic tumour associated with myasthenia gravis. Epithelial metaplasia was a conspicuous characteristic and was accompanied by scarcity of the corpuscles of Hassall. This accords with the observations of Bell, Lievre and Norris who reported that the thymic tumours which occur in patients with myasthenia gravis are of a distinct type and represent varying conditions of epithelial metaplasia. The more recent report of Obiditsch and Sloan, on the other hand, is contradictory and notes the predominance of lymphoid tissue to be found in such cases. Homburger considers that the co-existence of the thymic tumour with myasthenia gravis is significant because both diseases are rare. The tumours were also morphologically different from the thymic tumours which were not associated with myasthenia gravis. In the author's series 3 cases of carcinoma and 3 cases of persistence of the thymus gland in association with toxic goitre were found. In 6 instances the thymic lesion was an incidental finding at necropsy. There was moderate epithelial metaplasia in all thyrotoxic subjects, but metaplastic changes were rare in those patients in whom enlargement of the thymus gland was observed incidentally at post-mortem examination.

Tumours

Macrogenitosomia associated with enlarged thymus gland.—Precocious sexual and bodily growth, or macrogenitosomia, is divisible into the obese and the muscular, or 'infant Hercules', types. Weber and Wohl depict a case of muscular type associated with an enlarged thymus gland. Of the obese type the Cushing and the Leyton-Turnbull-Bratton syndromes are variations. In Cushing's syndrome Crooke found hyaline degeneration of the basophil cells of the anterior lobe of the pituitary gland, sometimes but not always associated with the adenomas described by Cushing. In the Leyton-Turnbull-Bratton syndrome, of which the characteristic is neoplasm of the thymus gland, he found similar hyaline pituitary degeneration associated. Of other endocrine abnormalities leading to precocious obesity hypernephromas are outstanding. The muscular type of precocity has hitherto been associated with testicular growths, hypernephromas and cerebral tumours near but not always involving the pineal body. In the patient described, a boy of 14 years of age, sexual and muscular precocity appeared at the age of 11. A tumour of the superior mediastinum was diagnosed as a persistent hypertrophied thymus gland or a thymic neoplasm. A naevus unius lateris involved the left trunk and upper limb. All other systems were normal. Two alternatives emerge, first that

precocity, enlarged thymus gland and naevus were coincident independent developmental anomalies or secondly that the precocity arose from the enlarged thymus gland. Probably the second hypothesis is true and the thymus is veritably an endocrine gland. If this is admitted muscular precocity originating in the thymus gland may constitute a new syndrome.

Homburger, F. (1943) *Arch. Path.*, **36**, 371.

Weber, F. P., and Wohl, M. (1944) *Med. Pr.*, **211**, 22.

TONSILS DISEASES

See also B.E.M.P., Vol. XII, p. 40; Interim Supplement, No. 11*; and Cumulative Supplement, Key Nos. 1484–1488.

Acute tonsillitis

Treatment

Curtailment of the course of the disease.—Apart from complications such as peritonsillar abscess or nephritis, acute tonsillitis is self-limited to a week or 10 days. It may be curtailed to less than 48 hours, according to Stovin, by the use of bismuth suppositories per rectum. Salicylates and other antipyretic drugs are palliative, not curative. The predominance of streptococci, as compared with the staphylococci, pneumococci and Vincent's organisms also commonly present, warranted the trial of sulphonamides but they have proved to be disappointing and even deleterious. Since 1941 soluble bismuth compounds or the insoluble suspension in oil have been employed intramuscularly in catarrhal, follicular and parenchymatous tonsillitis with benefit, but they present the disadvantages of painful injection, induration and possible abscess formation. The suppositories which are now advocated are devoid of toxicity. Each contains 0.135 gramme of the rectally absorbed bismuth salt of heptadiene-carboxylic acid, equivalent to 0.045 gramme of metallic bismuth, in cocoa butter. For children half that amount is suitable. Deductions are based on 40 cases, 10 of which are described. Of these 10 cases, 4 illustrate the effect of bismuth in acutely infected tonsillar tabs and granulations which had persisted after tonsillectomy. Another case illustrates the probable abortion of a peritonsillar abscess. A sixth case portrays the rapid response of a child who was acutely ill at the age of 22 months. Two suppositories usually suffice.

Removal of tonsils

Operative technique

Bloodless tonsillectomy in adolescence.—Procaine hydrochloride in the form of novotox (procaine with isoctylhydrocupreine hydrochloride) is the main anaesthetic used by Morey when he performs tonsillectomy. Free injection produces perfect anaesthesia and haemostasis is either absolute or only allows the loss of rarely more than an eggcupful of blood. Moreover bulky injection elevates the tonsil in its bed. In Morey's cases, 40 minutes before operation the patient received morphine and atropine and 10 minutes before operation equal parts of 10 per cent cocaine and adrenaline 1 in 1,000 were sprayed on the throat. For the purpose of injecting the tonsils a 20 cubic centimetre Record syringe was employed which carried a reinforced 5-inch needle which was bent nearly to a right angle at the tip. Each tonsillar area received 5 injections of 5 cubic centimetres of $\frac{1}{2}$ per cent novotox. The sites of the first 2 injections were the top and the middle of the anterior faucial pillar; the third and most important injection entered the junction of the anterior pillar and the tongue. The fourth and fifth injections penetrated behind the posterior pillar as high and as low as possible. Ten minutes elapsed before the operator drew forward the tonsil with the volsellum. The incision started from below and traversed the free edge of the anterior pillar as far as the base of the uvula, and then down the edge of the posterior pillar for the space of one inch. Blunt dissection during gentle traction, attention being paid to absolute separation from the lower extremity of the anterior pillar, preceded removal with the snare. The patient's comfort and early return to employment, the rarity of secondary haemorrhage and the economy of the surgeon's and hospital's time are advantages of this procedure. The method is reserved for patients who are 17 years of age or older.

Associated outbreaks of poliomyelitis

Factors responsible.—Howard in Cincinnati has been investigating the relation of poliomyelitis and tonsillectomy with especial reference to the correspondence of the optimum time of the year for performing the operation—late summer and early autumn—and the peak incidence period of the disease. He states that since 1910 it has been increasingly noted in the United States of America that in years in which poliomyelitis was epidemic there appeared to be a distinct susceptibility in children who had recently had their tonsils and adenoids removed to contract the disease, often in a lethal form. It was recorded in 1929 that in a group of 714 patients with the disease 30 per cent had undergone the operation within the previous year. Statistical tables drawn up by independent observers show that if the onset of the disease is within 30 days of the operation it is predominantly of the bulbar or bulbo-spinal type, whereas if from 30 to 60 days have elapsed it is more likely to be of the rather milder spinal variety. It used to be thought that the portal of entry of the causal organism—a filtrable virus—was the olfactory tract but as the result of recent experimental work on monkeys it is now generally considered to be through the mucous membrane of the alimentary tract, upper or lower, whence it is conveyed to the spinal cord through the sympathetic nerve fibres. An

experiment demonstrated that if the virus was injected into the tonsillo-pharyngeal region in monkeys 80 per cent contracted the disease, whereas if the virus was injected subcutaneously the disease did not develop. It is stressed that operations on the nose and throat, especially on tonsils and on adenoids, should in epidemic years be postponed until after the summer months at least, and reference is made to the possibility that non-susceptible individuals may act as 'carriers' and to the advisability of taking the usual precautions against infection. The conclusion comes to is that in non-epidemic years the possibility of poliomyelitis after tonsillectomy and adenoidectomy is minimal, though not altogether negligible, if undertaken during July, August, September and October, whereas if it is performed during the other eight months of the year the risk is practically nil.

Howard, R. E. (1944) *Ann. Otol., etc., St. Louis*, **53**, 15.

Morey, G. W. (1943) *Lancet*, **2**, 794.

Stovin, J. S. (1944) *Arch. Otolaryng., Chicago*, **39**, 259.

TORTICOLLIS

See also B.E.M.P., Vol. XII, p. 48.

Types

Spasmodic

Review of treatment.—Patterson and Little analyse 103 cases of spasmodic torticollis conforming to their specification of tonic or clonic spasms of the neck musculature producing abnormal deviation of the head, the chin being rotated to one side or the head bent directly forward or backward. The average age of onset, usually insidious, was 38 years, sex and occupation appearing to be immaterial. The sternomastoid was involved on the side to which the chin deviated in 19 per cent of cases and in 47 per cent on the opposite side. The arm muscles, trapezius, semispinalis and splenius capitis posticus were often concerned, and other muscles participated sporadically. An organic rather than a functional origin is suggested by the parallel curves of incidence of torticollis and encephalitis, by the comparative failure of psychotherapy and by the prevalence of vestibular symptoms. The effect of posture is also evidence of the relation to the vestibular tracts which, with the extrapyramidal tracts, the corpus striatum and the caudate nucleus are the neural elements probably concerned. A summary of treatment shows that mechanical, local and physical therapy employed for 100 patients was ineffective in 56, produced slight improvement in 35, much improvement in 7 and 2 recoveries. Systemic treatment of 56 patients, including the giving of drugs and vitamins and the adoption of dietary measures, was ineffective in 38 cases and produced slight improvement in 16 and much improvement in 2 but not any recoveries. Psychological treatment produced 2 recoveries in 41 patients, slight improvement in 12 and much improvement in 2; 25 were not benefited. Surgical measures, excluding myotomy which proved useless in 7 cases, were more advantageous. Two patients were much improved by unilateral extradural section of the cervical roots. Unilateral section of the spinal accessory nerve was carried out in 19 cases and the operation was a failure on 7 occasions but produced minor improvement in 8 cases and major improvement in 3; there was 1 cure. As a result of the intradural operations there was minor improvement in 3 and major improvement in 8 cases; 4 failures and 1 cure are reported. The prognosis is not good but 10 per cent only of patients later reported complete inability to work.

Patterson, R. M., and Little, S. C. (1943) *J. nerv. ment. Dis.*, **98**, 571.

TOXICOLOGY: INDUSTRIAL POISONING

See also B.E.M.P., Vol. XII, p. 127; Interim Supplement, No. 10*; and Cumulative Supplement, Key Nos. 1528–1540.

Prevention of disease in industry

Investigation of toxic materials

Physiological investigations.—Goldblatt deals with the work of the industrial doctor in the investigation of toxic hazards. There are four methods of discovering the physiological properties of toxic materials. (1) A search of the literature is clearly indicated as a method but alone it is rarely sufficient. (2) The physical and chemical properties of the substance may be ascertained from observations personally conducted by the doctor in charge aided by suitable technicians. (3) Experimental studies prove to be of great value but conclusions are often beset with incongruities, as the action commonly differs in man from that which occurs in the experimental animal. Goldblatt emphasizes the importance of the skin, which is secondary only to the lungs, as a route of entry of toxic products. The condition of the skin itself influences the outcome. It is relatively easy to determine in an animal the risk of absorption via the skin. (4) Clinical investigation is the fourth method. The author points out that clinical study was overshadowed by 'the business of compensation' until recently, but that it is now less difficult to institute periodical clinical examinations. Much tact is required since, if the idea that the material is dangerous are suggested to the worker, considerable difficulties may arise.

Toxic cases

Irritant gases

Fluorine and its compounds.—The incidence of fluorosis in industrial workers and the effects

of fluoride in the diet of human beings have already been studied by various observers. Largent, Machle and Ferneau have investigated the bone changes which occur in experimental animals fed on a diet containing sodium fluoride and cryolite. X-ray films, chemical analyses and macroscopic and microscopic examinations were employed and control studies were made. Fluoride salts were given to rabbits in doses of from 12 to 50 milligrams per day for from 16 to 92 days. The animals were then killed and the bones were analysed for the fluorine content, which was found to be high in all the treated animals. The X-ray films failed to show early osseous changes but macroscopically areas of porosity were seen to be scattered throughout the various bones. Much of the skeleton showed a chalky appearance and bone deposits were seen in many cases on the mandible and on the long bones. There was also a characteristic swelling of the mandible. The new bone formation was similar in structure to callus which formed after fractures had been produced experimentally in some of the animals. Microscopical examination of the porous areas and exostoses showed that the hyperplastic areas were true bone and not merely deposits of mineral salts. It appears that small deposits, areas of hyperplasia and early exostoses may be produced in animals by the ingestion of fluoride compounds without their being demonstrable by radiological examination. It is possible that similar deposits may also occur in the case of industrial workers. It also remains to be determined whether or not disability or limitation of movement may occur before bone changes can be detected on X-ray films. The authors suggest that radiological examination of the mandible may be useful in the detection of early osseous changes due to fluorosis in human beings.

Benzene and its homologues

Clinical picture of benzene poisoning

Effects of exposure to toluene fumes.—For some years Wilson has studied the effect of exposure to toluene (methylbenzene) fumes on employees in a large industrial plant. The absorbed fumes have a depressant action on the central nervous system and the bone marrow. The action is narcotic, but toluene is also an irritant to mucous membranes. Susceptibility varies but exposure to concentrations of over 500 parts per million for from 1 to 3 hours is always dangerous. In Wilson's series of approximately 1,000 employees who were exposed to the fumes there were not any fatalities. The chief symptoms, according to the concentration of the fumes and to the time during which the exposure lasted, were headache, lassitude, nausea, anorexia, incoordination, delayed reaction, palpitation and extreme weakness. The blood picture was mostly normal except for a drop in erythrocytes to 2,500,000 per cubic millimetre; 10 per cent showed this change. There was occasional decrease of polymorphonuclear cells and of reticulocytes with increase of mononuclears. In 2 cases the bone marrow showed partial destruction of blood-forming elements; these responded well to whole blood transfusions. Rest was necessary in all cases and all the patients were given a first class diet. Symptoms due to depression of the central nervous system disappeared gradually after several weeks of rest but weakness and anaemia persisted for months. It is recommended that free toluene fumes should not be allowed to exceed 200 parts per million; adequate ventilation is necessary to ensure this. Frequent examination of workers should be made; the blood count should be done and if necessary biopsy of sternal marrow should be carried out.

Nitro- and amino-derivatives

Trinitrotoluene

Experiments in detoxification.—Smith, Westfall and Stohlman have carried out experiments on rats, guinea-pigs, rabbits and cats for the purpose of inducing trinitrotoluene poisoning and subsequently of attempting detoxification. The susceptibility of different animals to trinitrotoluene varies and the metabolic changes undergone by the compound also appear to differ in different animal species. A knowledge of the factors which influence susceptibility and metabolic changes may provide means for the control of the toxicity of trinitrotoluene. Possibly some of the metabolic products in the body may be detoxified by glycuronic acid and since both glycuronic acid and ascorbic acid detoxify phenol, it is possible that ascorbic acid may play an important part in the mechanism of detoxification of trinitrotoluene. An increased excretion of urinary porphyrin has been reported in human subjects exposed to trinitrotoluene and therefore the urinary excretion of porphyrin in the experimental animals used in the investigations was also studied. It appeared that ascorbic acid had little influence on states of chronic poisoning, except in the case of cats, which are highly susceptible to trinitrotoluene; in this group the animals who received ascorbic acid outlived the control animals and there was less reduction in the haemoglobin content of the blood. The elimination of the reduced products of trinitrotoluene or of porphyrin compound was not affected by ascorbic acid administration. The incidence and severity of fatty degeneration of the liver in the animals observed indicated that the degree of degeneration varied in accordance with the dosage and the duration of poisoning rather than with the particular susceptibility of any species.

Goldblatt, M. W. (1944) *Brit. J. industr. Med.*, **1**, 20.

Largent, E. J., Machle, W., and Ferneau, I. F. (1943) *J. industr. Hyg.*, **25**, 396.

Smith, M. I., Westfall, B. B., and Stohlman, E. F. (1943) *J. industr. Hyg.*, **25**, 391.

Wilson, R. H. (1943) *J. Amer. med. Ass.*, **123**, 1106.

TRACHEA DISEASES

Sec also B.E.M.P., Vol. XII, p. 200.

Infective granulomas*Tuberculosis*

Treatment of tuberculous tracheobronchitis.—The following method of treatment for tuberculous tracheo-bronchitis complicating pulmonary tuberculosis is advocated by Davies. (1) Complete rest in bed in a sanatorium; (2) warm, damp atmosphere, adequate fluid intake, postural drainage, expectorants if necessary; (3) regular bi-weekly bronchoscopic cauterization of all accessible ulcerating lesions with silver nitrate 30 per cent; (4) collapse therapy if a main or lobar bronchus is seriously obstructed and if the obstruction cannot be promptly relieved—complete thoracoplasty is usually the measure of choice; (5) radical surgery in exceptional cases. Of the author's 26 patients one died and in 7 the disease was arrested. Visible lesions disappeared in 23. In a control group in which local treatment was not employed the result appeared to be worse but both groups were too small to lend themselves to statistical treatment. The treatment is unsuitable in the following cases because bronchoscopy is contra-indicated. (1) Severe tuberculous laryngitis, especially if acute, (2) acute respiratory infections, (3) recent haemoptysis and (4) grave general condition. Healing of circumferential ulceration is likely to be followed by stenosis requiring bronchoscopic dilatation. At least 2 months should be allowed to elapse after healing is complete before dilatation is undertaken, unless toxæmia from retained secretions demands relief.

Davies, R. (1943) *Amer. Rev. Tuberc.*, **48**, 94.

TRACHOMA

Sec also B.E.M.P., Vol. XII, p. 209; Interim Supplement, No. 12*; and Cumulative Supplement, Key No. 1545.

Treatment*Treatment of sequelae*

Operation for trachomatous entropion.—An operation for trachomatous entropion devised by Cockburn and performed with satisfaction in 60 cases consists in the following steps. (1) Blocking of supra-orbital and frontal nerves and infiltration of eyelid with novutox-adrenaline solution is carried out. (2) A Desmarres's forceps is applied to the eyelid and tightened sufficiently to secure a bloodless field. (3) The skin is incised parallel to and about 5 millimetres above the lid margin. The incision is undermined on each side to expose the orbicularis fibres. The tarsal plate is cleaned of all overlying tissue and a horizontal strip of it about 2 millimetres wide and extending right across the plate is excised. Sutures are inserted, passing through the skin of the inferior lip of the wound and deep into the upper lip of the tarsal plate. The ends are left long and secured to the brow by strapping. The upper lip of the skin flap is left undisturbed.

Cockburn, C. (1943) *Brit. J. Ophthalm.*, **27**, 308.

TRAVEL-SICKNESS

Sec also B.E.M.P., Vol. XII, p. 222.

Aetiology*Stimuli of seasickness*

Chronic seasickness in the United States Navy.—Schwab classifies the stimuli which give rise to sea sickness in different individuals as psychic, olfactory, visual, vestibular, gastrointestinal and proprioceptive. He divides sea sickness in the United States Navy into three types. Type (1) is prone to every form of motion sickness, in trains, cars, elevators, swings and the like. Of such individuals 74 per cent possess neurotic dispositions. Many went through early life comfortably by avoiding or leaving the kind of conveyance that made them feel ill. When they join the Navy they cannot do so. Sea sickness persists, they lose weight, and efficiency ranges from zero to 20 per cent. Their sense of inadequacy produces psychoneurosis. As sea sickness carries the stigma of weakness or disgrace, the sympathetic medical officer often invalids the sufferer, otherwise labelled, to hospital. Here such patients follow one of 3 courses. (1) A few desert. (2) many develop complaints unrelated to sea sickness and (3) some plead, tearfully or belligerently, for employment ashore. Neurotic symptoms persist while the possibility of sea service remains. Employment ashore or discharge are the only alternatives. Barium fluoroscopy showed gastro-intestinal abnormality in 50 per cent of sufferers. Individuals coming on land after weeks of sickness at sea displayed duodenal and pyloric irritability which led to spasm, gastric hypersecretion, increase of the gastric rugae and diminished peristalsis. Type (1A) although prone to motion sickness show less loss of weight and greater efficiency. In quiet waters or in a big ship they have a moderate success. Type (2) is without history of motion sickness. Although susceptible to rough weather they lose little weight and can work with somewhat reduced efficiency.

Schwab, R. S. (1943) *Ann. intern. Med.*, **19**, 28.

TROPICAL ULCER

See also B.E.M.P., Vol. XII, p. 256.

Diagnosis*X-ray appearances of bone*

Four clearly marked groups.—Brocklebank describes the radiological appearances in bone in cases of tropical ulcer of the lower part of the leg. This tropical ulcer or phagedaenic ulcer must be distinguished from Delhi or tropical sore, and from veldt sore (diphtheria). It may affect any part of the body, but is far more often seen on the feet and lower part of the legs. It starts as a painful pustule which rapidly forms a spreading sloughing ulcer with a purulent discharge and it may involve muscles, tendons and bones. The radiological appearances of bone are divided into 4 groups which in the earlier stages of the disease can be quite clearly differentiated as follows. (1) Normal. In approximately 50 per cent of the cases in this series there were not any radiological changes. A point of interest is the difficulty of anticipating this on clinical grounds; several ulcers of large extent and apparent chronicity did not show any changes in the associated bones and some small, apparently recent ulcers were associated with advanced osseous lesions. (2) Local periostitis. The earliest radiological change demonstrated is a mild periosteal reaction limited to an inch or two of the bone at the site of the ulcer; it greatly resembles the reaction seen in Europeans with chronic varicose ulceration of the leg. (3) Local osteo-periostitis. This is a slightly more advanced stage. (4) Osteomyelitis. In this stage sequestrum formation occurs early and almost constantly. Diagnosis should be made from syphilis and yaws.

Brocklebank, J. A. (1943) *Brit. J. Radiol.*, **16**, 221.

TRYPANOSOMIASIS

See also B.E.M.P., Vol. XII, p. 263; and Cumulative Supplement, Key No. 1553.

Clinical picture and course*Ophthalmic disturbances*

Scott discusses the eye changes in trypanosomiasis. Keratitis and irido-cyclitis have been produced experimentally in animals. Among human beings, cases of keratitis, irido-cyclitis, choroïdo-retinitis and optic atrophy have been reported. One hundred and fifty cases of *Trypanosoma gambiense* infections (including 2 Europeans) were examined for eye changes. In only one case was keratitis attributable to the disease. The high incidence of trachoma in the district accounted for 31 of the 42 cases of keratitis. In the remaining 11 there was evidence of past keratitis which may have been due to sleeping sickness. Irido-cyclitis was an important complication and was found as the presenting sign in 4 of 26 hospital cases; 7 cases in all of irido-cyclitis were encountered. Cases of choroïdo-retinitis or optic atrophy due to the disease were not met with but one case of arsenical optic atrophy occurred after the eighth injection of trypanamide. In order to guard against arsenical optic atrophy, the author suggests the testing of the visual acuity with Landolt's rings before each injection in preference to perimetry.

Treatment*Curative*

Effects of pentamidine.—In sleeping sickness van Hoof, Henrard and Peel, of the Institut de Médecine Tropicale Princesse Astrid, Léopoldville, Belgian Congo, found that one appropriate dose of pentamidine (4 : 4'-diamidinodiphenoxypentane) rid the patient's blood of *Trypanosoma gambiense* as a rule by the third day. The appropriate dose of from 1 to 2 milligrams per kilogram of body weight, and the safest procedure—by injection twice weekly for 10 injections—were determined by experiment on infected guinea-pigs. Pentamidine proved to be equally potent against trypanamide-fast flagellates; intramuscular injection was less toxic and not less effective than intravenous injection was. In two early cases of infection clinical cure and a normal cerebrospinal fluid resulted. In the second patient however intolerance of pentamidine after the fifth dose compelled resort to trypanamide and Bayer 205 (suramin). In advanced cases in which there is involvement of the central nervous system clinical cure is unattainable although the trypanosome is readily extirpated. In such cases pentamidine should be reserved for patients in whom optic neuritis is to be feared or in whom the trypanosomes are arsenic-fast. Two native volunteers, who were freely bitten every 2 or 3 days during one year by infected tsetse flies, illustrated the prophylactic value of pentamidine. Each volunteer received one injection of 2 and 3 milligrams respectively per kilogram of body weight and acquired 1 year's immunity and 10 months' immunity respectively. Infected flies which were fed on pentamidine-protected animals were not disinfected and the cyclical development of their parasite was unaltered.

van Hoof, L., Henrard, C., and Peel, E. (1944) *Trans. R. Soc. trop. Med. Hyg.*, **37**, 271.

Scott, J. G. (1944) *J. trop. Med. (Hyg.)*, **47**, 15.

TUBERCULOSIS

See also B.E.M.P., Vol. XII, p. 286; and Cumulative Supplement, Key No. 1554.

Aetiology and bacteriology*The tubercle bacillus*

Resistance to artificial gastric juice and to duodenal secretion.—Floyd and Page report on the resistance of tubercle bacilli to artificial gastric juice and to duodenal secretions. Ten strains of virulent bacilli were employed. The artificial gastric juice contained pepsin 5 grammes, hydrochloric acid 6 cubic centimetres, lactic acid 2 cubic centimetres and water to 1,000 cubic centimetres. The duodenal contents were obtained from fasting young adults by the method of inserting a duodenal tube under fluoroscopic guidance. A portion of culture was ground in a mortar with 5 drops of 5 per cent taurocholate solution, 3 cubic centimetres of sodium phosphate buffer solution being slowly added. After settlement 1 cubic centimetre of supernatant fluid was added to a Hopkins tube and centrifugalized. Readings of 0.01 milligram were selected for dilution in the proportion of 0.001 milligram per cubic centimetre which has been calculated to contain 1,000,000 bacilli. One cubic centimetre from each strain was added to 15 cubic centimetres of gastric juice and was incubated at body temperature for a period of 3 hours. A second series of 10 preparations was incubated for a period of 6 and a third series for a period of 12 hours. In the fourth series bacilli were incubated for periods of both 6 and 12 hours with duodenal contents. In the fifth test bacilli were exposed first to gastric juice and then to duodenal contents. Guinea-pigs were injected with the sediments of the incubations. Macroscopical, microscopical and cultural observations after the lapse of 6 weeks showed that the 3-hour group was affected twice as severely as was the 6-hour group. The 6-hour group was 80 per cent more affected than was the 12-hour group. Massive lesions were absent and few bacilli were recoverable in smear or in culture. The duodenal content alone or supplementary to gastric juice was inoperative.

Channels of infection

Danger to children of exposure to active tuberculous infections.—The 65 admissions for tuberculosis to Great Ormond Street Children's Hospital, London, during the first half of 1942 constitute an increase of 41 per cent over the admissions during the first half of 1938. Harker suggests that the main factors which have led to the increase are the return home from hospitals and sanatoria of persons with pulmonary tuberculosis still active, the conditions of shelter life during air-raids and the exposure of evacuated children to infected milk supplies. Miliary tuberculosis shows remarkable increase from 9 cases to 15 cases of which 4 patients were over 4 years old and the remainder averaged 11 months. All except one died rapidly of meningitis. Pulmonary infections excluding miliary infiltrations were nearly doubled. Most of these 23 patients were sent to sanatoria. Three showed erythema nodosum. Of 6 cases of abdominal tuberculosis one patient required operation for obstruction and 5 displayed distended abdomens, palpable glands and omental involvement. Satisfactory progress is reported in all. Joint and bone showed 7 infections of which 5 were spinal. All were referred to orthopaedic centres. The drop from 22 such infections in 1938 to 7 in 1942 is more apparent than real. The admission of chronic cases in 1938 had to yield in 1942 chiefly to admission of cases of acute disease. The result of the tuberculin reaction recorded in 40 patients was 36 times positive and 4 times negative. A history of contact was obtained in 11 cases. A thorough understanding on the part of the public of the danger of exposing children to contact with persons actively tuberculous is urgently needed.

Prognosis*Erythrocyte sedimentation rate*

Is its value overestimated?—Banyai and Cadden discuss the results of the erythrocyte sedimentation test as applied to 2,640 tuberculous patients at Muirdale Sanatorium, Wisconsin, for a period of 4½ years from 1939. Many theories have been advanced in explanation of the changes in the sedimentation in health and in disease, but there is not any doubt that the rate is subject to the Stokes physical law regarding the sinking of particles suspended in a fluid medium. The equation is $V = \frac{2}{9} g \frac{S - S_1}{\mu} r^2$, when V is the velocity of the fall, g the gravitation constant, S the specific gravity of the erythrocytes, S_1 the specific gravity of the blood plasma, μ the absolute viscosity of the plasma and r the radius of the erythrocyte aggregates. It will be noted that the right side of this equation contains four variables. Normally, erythrocytes settle faster in women than they do in men and the rate is increased by pregnancy, menstruation, exercise, hunger and old age; it may even be affected by the weather. It is therefore a test with many limitations and according to these observers compares unfavourably with serial radiographs of the chest. In 8 per cent of the 2,640 cases under review it was found to be normal.

Diagnosis*Detection of tubercle bacilli*

Fluorescent microscopy.—Graham publishes the results of his investigations into the factors governing fluorescent microscopy of the tubercle bacillus. Recent reports on this method of recognition claim that, as compared with the Ziehl-Neelsen method, it saves time and gives an

increase in the number of positive findings, especially in the examination of gastric concentrates; it is admitted however that cultural methods are more sensitive than either of the two. Guinea-pig inoculation is not mentioned. The advantage of the fluorescent method of examination lies in the fact that low magnification must be used. An 8-millimetre objective and 10X ocular, which give a field of 4 or 5 times the area given by $\frac{1}{8}$ -inch oil immersion, are employed. The dyes used are auramine or thioflavine. Auramine stains acid-fast bacilli a faint yellow without the application of heat and the stained bacilli fluoresce when irradiated with violet or ultra-violet light. Films are fixed by heat in the usual way and are stained in the cold for 2 minutes with a freshly made aqueous saturated solution of auramine without any addition of phenol. The slide is rinsed in running water and decolorized for 30 seconds with Gabbett's methylene blue (2 grammes in 100 milligrams of 25 per cent sulphuric acid), then rinsed and examined dry without the use of immersion oil as soon as possible in a darkened room. With a suitable microscope and light the bacilli show up as fluorescent rods. By the use of a yellow filtering disk in the ocular the surrounding ground is rendered dark. There are many technical difficulties. The excitation band of auramine in the spectrum is in the neighbourhood of a wave length of 4-500 Ångström units, which is in the long-wave ultra-violet. Light approximating this wave length may be obtained from a G.E. 500 watt 120 volt T-20 projection bulb by filtering through cupro-ammonium solution or from an open carbon arc. The least tinge of yellow in the optical system of the microscope condenser cuts out the exciting light. The glass of many apochromatic microscope lenses contain fluorite crystals which themselves fluoresce and render the examination futile.

Virulence of mammalian tubercle bacilli

Discussion of various strains.—Corper and Cohn state that the identification of the virulence or avirulence of mammalian tubercle bacilli is most difficult. The Lübeck disaster when the *Bacille-Calmette-Guérin* virus was used stimulated efforts towards a solution of the virulence problem. According to Calmette and his associates B.C.G. is a fixed virus but American and Canadian students claim to have found both virulent and avirulent dissociants in cultures of B.C.G. This is controverted by Behner and by the authors. An arbitrary label of the strain of mammalian tubercle bacilli is not a safe guarantee of virulence. The range of virulence of the different strains of H 37 (Baldwin), a human strain obtained from several laboratories, varied from avirulence to a very virulent grade. A human strain (Gluckson) isolated in 1920 remained partially virulent after artificial cultivation for over 20 years. It is interesting to note that laboratory cultures maintain a fairly stable virulence whereas some strains from human sputum vary from high grade virulence to avirulence. In determining virulence of mammalian tubercle bacilli the intravenous test in guinea-pigs with 1 milligram of fine suspension can be recommended. For extreme accuracy the test can be verified by graded subcutaneous tests. By storing desiccated bacilli in sealed glass tubes at refrigerator (3° C.) temperature virulence may be preserved for years.

Sero-diagnostic tests

Variations in serum calcium.—Since calcium is frequently advocated for the amelioration of tuberculous conditions, Rai and Kehar investigated the specific part played by calcium in tuberculosis. They studied the variations in serum calcium as affected by the various stages of the disease. The serum calcium in healthy Indians was determined, as figures obtained by workers elsewhere might not apply to India, in view of the differences in topography, climate, diet and heredity. The serum calcium of 49 healthy adults and of 275 tuberculous men and women living under similar conditions was estimated. The authors found that the average amount of serum calcium in men is 10.84 milligrams per 100 cubic centimetres of blood and in women 10.43 milligrams. A significant decrease is found in the case of men in the early, advanced, active and quiescent stages of tuberculosis, as compared with healthy persons. Between early and advanced cases however the differences in the averages for serum calcium are not significant in respect of either men or women. No significant decrease is found in tuberculous women patients in various stages of the disease as compared with the healthy state. Haemoptysis as judged from 15 cases does not seem to affect the level of serum calcium.

Skin tests

Mantoux test in children.—Fleming states that the incidence of positive reactions to the Mantoux test (1 in 1,000) in children admitted to the Royal Hospital for Sick Children, Glasgow, between and including the years 1938 and 1942 was as follows: aged under 4 years, 9.3 per cent; aged 4-7 years, 26.3 per cent; aged 7-10 years, 38.1 per cent and aged 10-13 years, 44.8 per cent. The figures agree fairly closely with those of other workers in assigning a place of special importance to human infection in childhood. Positive reactions have a much less grave significance in older children than in the very young: of a series of 767 children with positive reactions admitted to the hospital, 286 were under 4 years of age and 32.1 per cent of these died of tuberculous meningitis; 322 were over 7 years of age and only 5 per cent of these died of tuberculous meningitis. Great care should be taken to prevent contact between young children and adult carriers, and children giving positive tuberculin skin reactions should be placed under observation in suitable surroundings for about 6 months. Most of these children are not infectious, hence isolation need not be rigorous. For economic or other reasons institutional treatment is often advisable.

Banyai, A. L., and Cadden, A. V. (1943) *Arch. intern. Med.*, **72**, 245.

Corper, H. J., and Cohn, M. L. (1943) *Amer. J. Clin. Path.*, **13**, 352.

- Fleming, G. B. (1943) *Lancet*, **2**, 580.
 Floyd, C., and Page, C. G. (1943) *Amer. Rev. Tuberc.*, **48**, 174.
 Graham, C. F. (1943) *Amer. Rev. Tuberc.*, **48**, 421.
 Harker, Margaret E. (1943) *Lancet*, **2**, 387.
 Rai, B. B., and Kehar, N. D. (1943) *Indian J. med. Res.*, **31**, 183.

TYPHUS FEVERS

See also B.E.M.P., Vol. XII, p. 325; Interim Supplement, No. 16*; and Cumulative Supplement, Key Nos. 1558-1560.

Epidemic or louse-borne typhus fever

Clinical picture and course

Apparent prevalence of 'influenza'.—McConn publishes observations on an epidemic of typhus fever which occurred in County Galway, Eire, in 1942. For the last 50 years in this district the disease has invariably been initiated in aberrant forms, although a constant watch is kept for possible outbreaks. In Spiddal, West Galway, during the winter of 1942 an outbreak of typhus fever occurred after a free interval of 40 years had elapsed. The first 2 patients showed the typical clinical features of broncho-pneumonia, and both recovered without typhus being suspected. The third patient presented symptoms of a pelvic abscess, but the case was correctly diagnosed before an operation was undertaken. Investigation of the district demonstrated the apparent prevalence of 'influenza' associated with symptoms of headache, lethargy and conjunctivitis and a slaty-blue abdominal rash; schoolchildren especially were affected and in some cases there was a generalized mottled rash simulating louse-bites. Suspected victims were removed to hospital and Weil-Felix tests were carried out on every contact and suspect in the district. Five hundred and thirty-five persons were thus examined out of a population of 2,222; of these, 14 were ill with typical typhus. More than half of the 535 patients had verminous heads and more than one-third had body lice. A comparison of Weil-Felix test results in non-typhus areas was made in Connemara. The authors consider that a Weil-Felix test which gives a reaction of 1-50 to a *Bacillus proteus* OX 19 suspension, when associated with symptoms of a cold or mild influenza, should be regarded as diagnostic of typhus fever, and that all possible precautions should be taken until a second test has been made some days later. The Weil-Felix reaction does not disappear entirely in less than 6 years, and a second attack of the disease is possible. Two such cases were noted in the 1942 Spiddal epidemic.

Diagnosis and differential diagnosis

Incidence of agglutinins for Proteus OX 19, OX 2 or OX K.—In the investigation into the incidence of agglutinins for *Proteus* OX 19, OX 2 and OX K reported by Penfold, a vaccine prepared by the Connaught Laboratories, Toronto, from a European louse-borne strain of *Rickettsia prowazeki* grown in the yolk-sac of chick embryos was used. With a vaccine made at the same date Felix obtained a definite increase in OX 19 agglutinin titre in about half the number of the persons inoculated. Twenty-three persons were vaccinated at weekly intervals; each received 0.25, 0.5 and 1 cubic centimetre of vaccine; 3 months later a further dose of 1 cubic centimetre was given. The Weil-Felix reactions of these persons showed low normal agglutinin titres. Vaccination in the majority of cases resulted in an increase in titre of the 3 agglutinins. Three months later they had decreased somewhat, but after revaccination whereas the OX 19 and OX 2 agglutinin titres rose again the OX K titres were not appreciably altered. If more than 100 per cent increase in OX 19 agglutinin titre is taken as significant, 14 cases of 23 showed such an increase after primary vaccination and 17 after revaccination. General reactions to the vaccine such as headache or malaise were less common than were local reactions, which however subsided in a day or two.

Non-epidemic or epizootic typhus fevers

Flea-typhus

Effect of V147.—Andrewes, King, van den Ende and Walker consider the activity of *p*-sulphamidobenzamidine hydrochloride (called V147) and its corresponding amidoxime (V186) and other related substances against typhus rickettsiae in mice. The experiments mainly concerned murine typhus fever but they were corroborated by the effect of V147 on the Breinl epidemic form and on forms encountered in Tunis. The method of intranasal passage which was elaborated to adapt these organisms to the infection of mouse lungs is described. From lungs which were successfully infected a stock of rickettsiae was prepared by pounding the lung in horse serum. After centrifugalization the supernatant fluid was stored at 77° C. Mice were inoculated nasally with 0.05 cubic centimetre of this suspension in progressive tenfold dilutions and were killed a week later. By counting with lens or naked eye the discrete foci on the lung surface (necessarily neglecting the foci in the lung substance) a quantitative estimation of the effect of a known dosage of the suspension was made. Experiment next determined that the maximum dose of V147 was 4 milligrams, that 2 doses per diem were desirable and that the drug was more effective when introduced before than several hours after infection. On the first day one intraperitoneal dose of 4 milligrams of V147 was given, after which intranasal infection with the typhus suspension was carried out. Two doses of V147 on the second and third day were followed by one dose on the fourth day.

Inspection of the mice when they were killed a week after infection showed that all suspensions to the (10⁻⁴) dilution had infected the controls without infecting the medicated animals. Subcutaneous and alimentary administration of V147 also proved to be effective. Similar results were attained with *p*-sulphonamidobenzamidoxime hydrochloride (V186) but otherwise action is peculiarly specific and is confined to substances closely allied to V147. These compounds, which lack the direct attachment of a nitrogen atom to the ring, do not conform to the sulphonamides. Clinical trial in North Africa and Naples has proved to be profoundly disappointing.

Andrewes, C. H., King, H., van den Ende, M., and Walker, J. (1944) *Lancet*, **1**, 777.

McConn, C. F. (1943) *Lancet*, **2**, 535.

Penfold, J. B. (1944) *Brit. med. J.*, **1**, 114.

URETHRA, DISEASES

See also B.E.M.P., Vol. XII, p. 386.

In female

Injury

Stress incontinence.—Graber discusses the cause and care of acquired urinary stress incontinence in women who have borne children, particularly at the menopause. The female urethra is chiefly dependent upon the middle sphincter (sphincter urethrae membranaceae) for voluntary control of micturition. Hence the first principle in treatment is repair of this sphincter. Damage to the trigone muscle of the bladder is fortunately rare but injury to it may cause some incontinence and the ordinary repair may not correct the distressing symptoms. Distortion of the urethra must be corrected in order to cure incontinence completely. A stretched urethral lumen may produce incontinence. The author states that for successful repair certain principles are necessary. The calibre of the urethra must be reduced, the torn sphincters repaired, the urethra replaced in its normal position and adequate support for the repair provided.

Phaneuf, Heffernan and Kasdon report their experiences of Kennedy's operation which is designed to relieve the urinary incontinence that originates in parturition. Kennedy considers such incontinence to arise from injury to the inner and middle thirds of the urethral sphincter which leads to fine adhesions to the postero-lateral margins of the pubic rami. There is also rupture of the voluntary fibres which, running under the middle third of the urethra from ramus to ramus, constitute a sling support. His operation aims first at freeing the urethra by division of the adhesions restraining the involuntary sphincter and secondly at converting the voluntary fibres into a circular sphincter. First, an incision is made through the anterior vaginal wall and then the wall is dissected from urethra and bladder. The urethra is separated from the pubic rami, the separation extending into the paravesical space. Next, with 3 mattress sutures the sub-urethral tissues are plicated and tied and the urethra is thus withheld from forming fresh adhesions to the rami. The separation is reinforced by a second row of 3 sutures which approximate the fascia-like structures on each side of the urethra. Then the excess of the vaginal wall, and simultaneously the damaged portion of the voluntary sphincter, is resected. Sutures beginning at the highest point of the vestibule approximate the intact voluntary fibres of the sphincter and constrictor urethrae and close the vaginal wall. An indwelling soft rubber catheter is introduced for a period of 7 days. The authors' series comprises 23 patients of whom 17 received other simultaneous surgical treatment. An average period of 17 months' observation shows 18 cases of recovered control; 3 were much improved. Although 16 patients gave a history of incontinence exceeding a period of 4 years there were 2 failures only. Nevertheless, the duration of the incontinence is important and perhaps a patient who has had incontinence and cystocele for a period exceeding 5 years, needs more than an anterior colporrhaphy.

Frequency and its implications

Aetiology.—McKim, Smith and Rush discuss painful and frequent micturition in the female when urinary infection is absent. In 202 patients urethral caruncle was responsible, the bladder urine in 111 being infected. These were eliminated as they have been considered elsewhere and attention is drawn to 152 other cases. Seventy patients exhibited cystic degeneration of the mucosa at the vesical orifice. Such cysts are single or multiple, bullous or pedunculated. The bullous type with rounded elevations beneath a thin mucosa was shown in 26 patients and 44 displayed pedunculated cysts. Frequency was common to all patients and intermittent retention to 3 having pedunculated cysts. The origin of the cysts is unknown. Cauterization with the high frequency spark under observation and with low spinal anaesthesia was practised. The next large group consisted of conditions referable to the gynaecologist, fibroids, procidentia, uterine malpositions and cystoceles constituting the majority. Study of the next group comprising 18 cases of interstitial cystitis with uninfected urine showed a urinary hydrogen ion concentration consistently above 6, control of which by administering acids reinforces treatment. The bladder is invariably contracted and haematuria readily follows overdistension. Gradual dilatation by the gravity method and the use of silver nitrate solutions in increasing strengths adapted to the patient's tolerance gave the best results. In 8 cases vesical irritation was traced to volatile oils which had been absorbed by the respiratory or

digestive tract. Similarly one patient gained relief on ceasing to take barbiturates. To another group citrus fruit juice was irritant. It was found accidentally that injudicious smoking was a cause of irritation: it was facetiously suggested to a patient without physical signs that she change her brand of cigarette; relief ensued within 48 hours. Since this surprising result 7 similar patients have obtained speedy relief by taking the same action.

Graber, E. A. (1944) *Urol. cutan. Rev.*, **48**, 133.

McKim, G. F., Smith, P. G., and Rush, T. W. (1943) *J. Amer. med. Ass.*, **123**, 603.

Phaneuf, L. E., Heffernan, R. J., and Kasdon, S. C. (1943) *New Engl. J. Med.*, **229**, 743.

UROGENITAL ORGANS, ABNORMALITIES

See also B.E.M.P., Vol. XII, p. 401.

Urethra

Hypospadias

Treatment by two-stage operation.—Interferences with the genital and the excretory function call for surgical correction in hypospadias, according to Wehrbein, and the surgeon is handicapped by the septic site and by an untrustworthy collateral circulation. Operative procedure in two stages is advocated. The first aims primarily at correction of the ventral curve of the penis, always present but embryologically unexplained, by the method of freeing the corpus cavernosum. The steps of this procedure are (1) incision from the glans penis to the aberrant meatus, (2) freeing by dissection of the corpus, (3) undermining of the meatus, which retracts and (4) lateral nicking of the edges of the skin incision in order to allow its closure with fine silk sutures. In the author's operations a catheter was inserted for a period of 4 days and a firm dressing was applied in order to maintain the penis against the pubes. Simultaneously a pedunculated skin tube was prepared for future use by buttonholing the prepuce transversely and suturing the cut edges. A second skin was prepared along the median scrotal raphe. The second stage was the construction of the urethral tube, as follows. (1) From one side of the tip of the penis an elongated U-incision was carried round the false meatus and up to the tip of the penis on the other side; (2) the edges of the U-shaped tongue of skin were dissected up; (3) over a small catheter inserted in the urethra the edges were moulded and were united with fine catgut which pierced the edges only, not the skin; (4) the prepared skin tubes were then employed in order to cover the wound. If the false meatus was midpenile, the preputial tube sufficed but if it was situated at the scrotal angle the scrotal tube was also required. Each pedicle of the preputial tube and the proximal pedicle of the scrotal tube was severed. The tubes were then slit open, adjusted over the wound and stitched. Drainage by suprapubic cystotomy for 14 days has been found to be essential. Because of the importance of asepsis dressings moistened with merthiolate (sodium ethylmercurithiosalicylate) were changed daily and sulphathiazole was administered for 8 days. Eight of 11 cases proved to be successful and defects in the remaining 3 were readily remediable.

Wehrbein, H. L. (1943) *J. Urol.*, **50**, 335.

UTERUS, DISEASES AND DISORDERS: DISPLACEMENTS

See also B.E.M.P., Vol. XII, p. 426; Interim Supplement, No. 20*; and Cumulative Supplement, Key Nos. 1581–1584.

Displacements

Retroversion

Use of the pelvioscope.—Under the title of pelvioscope Harrell describes a magnified trocar and cannula which suitably illuminated affords a view of the pelvic viscera and is designed specifically in conjunction with a special round-ligament hook, for the performance of Gilliam's operation. The pelvioscope is a cannula 11 centimetres in length and 1 centimetre in diameter. The pointed trocar projects 4 centimetres below the cannula. A tube containing an electric bulb is adjustable by clamp below and beside the lower orifice of the cannula. The round ligament hook is a steel rod which tapers to end in a flattened hook. Heavy pre-operative medication renders local anaesthesia possible but spinal or general anaesthesia is preferable. With the patient in an exaggerated Trendelenburg position, a horizontal skin incision of 1 centimetre is made 3 centimetres above the symphysis pubis and 4 centimetres to the right or to the left of the middle line according to which ligament is first to be suspended. The procedure then is as follows. (1) Puncture of the abdominal wall with trocar and cannula; (2) withdrawal of trocar and confirmation that the peritoneum has been punctured. Otherwise re-insertion and rotary manipulation of the trocar is necessary; (3) introduction and clamping of the low voltage electric light; (4) identification of the round ligament and its encirclement with the hook; (5) elevation of the ligament to the fascial level; (6) withdrawal of the cannula over the hook; (7) seizure of the ligament with Allis's forceps and its suture to the fascia. Usually the punctures of fascia and skin do not require suture and the patient's confinement to bed is brief. The simplicity of procedure offers a solution to the surgeon who hesitates to advise a laparotomy when relief is less than certain.

Harrell, W. B. (1943) *Amer. J. Surg. N.S.*, **62**, 149.

UTERUS, DISEASES AND DISORDERS: PROLAPSE

See also B.E.M.P., Vol. XII, p. 436.

Treatment

Combined gynaecological and urological treatment

Potter and Low report on 317 operations for cystocele performed in cooperation with their hospital's urological department. Uterine prolapse and cystocele are commonly found to be interdependent as cause and effect. When childbirth leaves a retroverted uterus, a relaxed pelvic floor and the anterior vaginal wall torn from the cervix the condition is conducive to the occurrence of cystocele. Three types are usefully recognized, cystocele involving the entire base of the bladder and the rarer forms anterior or posterior to the interureteric bar. In the operations described the urological department was responsible for the localization of the cystocele and for the health of the urinary tract before and after operation; the choice of operative procedures was jointly determined. The surgical aim was anatomical restoration and mobilization of the bladder. Associated pathological conditions, tumours uterine and ovarian, endometritis and inflammations of the genital tract necessitated abdomino-vaginal operations in 150 cases. A modified Manchester procedure was employed in 60 cases. For complete procidentia, which occurred in 27 cases, vaginal hysterectomy was chosen and for 16 other patients past the fertile age the Watkin interposition operation. In 64 cases of suspected or known malignancy abdominal hysterectomy was performed, the correction of the cystocele being of secondary importance. One recurrence of cystocele is known to have occurred and the urological department has treated 38 cases of vesical difficulty none of which outlasted 3 months. The mortality rate was 0.6 per cent.

Surgical method

Age, possibility of future pregnancy, extent of prolapse, size of uterus and co-existent disease were considerations which influenced Phaneuf in determining the method to be used in performing 730 operations for uterine prolapse. Three degrees of uterovaginal prolapse constitute a practical classification. The first degree connotes appearance of the cervix at the vulva. Extrusion of the cervix is the second and total extrusion or procidentia the third degree. Conservative treatment during childbearing years is desirable. Pessaries relieve lesser degrees of prolapse. At this age procedures are standardized to trachelorrhaphy, repair of the vaginal walls and perineum; by the procedure of laparotomy the uterosacral ligaments are shortened and the uterus is suspended by the round ligaments. High cervical amputation and ventrifixation are avoided since they produce sterility, miscarriage or dystocia. After the menopause the latter operation is sometimes advisable for the purpose of correcting recurrence or of obliterating a large posterior vaginal hernia but vaginal methods predominate because their use incurs little morbidity and mortality. The interposition operation proved to be so satisfactory that it heads the list numerically with 224 cases. An atrophied uterus contraindicates this operation and vaginal hysterectomy with interposition of the broad ligaments takes precedence especially if cancer is suspected. The speed of the clamp method of hysterectomy recommends it for the aged. It is advantageous first to ablate the uterus and to repair the anterior vaginal wall with non-absorbable sutures and 3 weeks later to repair the pelvic floor. High vaginal fixation, excellent in first degree and second degree prolapse, is especially so in recurrences after vaginal plastic operations and ventrifixation in which the elongated uterus causes difficulties. The extraperitoneal Manchester or Fothergill operation grows in favour. Subtotal or total colpectomy, which is readily performed under local anaesthesia, is invaluable for the aged and infirm. The mortality throughout the series was 1.7 per cent. Spinal and local anaesthesia was employed in 230 cases.

Ring pessary

A case of incarceration and strangulation.—An unusual case of incarceration and strangulation of the cervix by the pressure of a rubber ring pessary which was worn for uterine prolapse is reported by McGoldrick and Lapp. Similar cases have occasionally been reported and all the patients have recovered after treatment. In the authors' case the woman, aged 48 years, had worn the ring pessary for about 4 weeks, with relief of the symptoms due to prolapse. Pain then developed in the lower part of the abdomen and slight vaginal bleeding occurred. On examination the cervix was seen presenting in the introitus. It was dark purple, oedematous and haemorrhagic and was swollen to about 5 times the normal size. The pessary could be palpated higher up in the vagina with the cervix herniated through the orifice. The patient was treated by a preliminary iced antiseptic douche in order to relieve the oedema. The pessary was then split in two places by means of a Liston osteotome and was extracted. The vagina was washed out with a warm permanganate douche immediately after the extraction and subsequently 3 times daily. Vaginal irrigations of sulphanilamide were also given. The patient's condition rapidly improved and only a small superficial area of sloughing was visible on the cervix. In about a week's time the cervix was completely healed and the patient was discharged.

McGoldrick, J. L., and Lapp, W. A. (1943) *Amer. J. Obstet. Gynec.*, **46**, 877.

Phaneuf, L. E. (1943) *Surg. Gynec. Obstet.*, **77**, 209.

Potter, S. B., and Low, H. T. (1943) *J. Urol.*, **60**, 322.

UTERUS, DISEASES AND DISORDERS: TUMOURS

See also B.E.M.P., Vol. XII, p. 448; and Cumulative Supplement, Key Nos. 1586-1590.

Fibroid tumours**Diagnosis and differential diagnosis**

Use of the culdoscope.—Decker and Cherry describe a new method, which they call culdoscopy, in the diagnosis of pelvic disease. Decker had found observation of the pelvic contents by a peritoneoscope through abdominal puncture to be unsatisfactory. This experience led to adoption of the vaginal route in order to view the pelvic contents. The culdoscope consists of a trocar and cannula specially designed for puncture of the cul-de-sac. A self-retaining cervical cannula with detachable tubing is essential, and a perineal retractor, a 20-cubic centimetre syringe and curved volsella are also required. With the patient in knee-chest position, supported by shoulder braces, upright leg-holders and thigh straps, and under caudal anaesthesia, a clear view can be obtained of the pelvic contents, and many intra-pelvic manipulations and procedures can be done. Culdoscopy is contra-indicated in certain pelvic and general conditions but Decker and Cherry consider it to be invaluable in the investigation of pelvic tumours, 'small ovarian disease', endometriosis and ectopic pregnancy and to be specially helpful in the detailed study of sterility in women.

Carcinoma**Significance of vaginal smears in early diagnosis**

Meigs, Graham, Fremont-Smith, Kapnick and Rawson have studied vaginal smears from 220 women in order to estimate their value in the diagnosis of carcinoma of the uterus. Cancer of the cervix and body of the uterus is curable if treatment is instituted early; delay in diagnosis is responsible for many deaths from this disease. A technically simple method of making a presumptive diagnosis would greatly aid the early discovery of female genital malignancy. The technique for taking the vaginal smears was that used by Papanicolaou. The normal cells of the vaginal secretion consist of the cornified types together with basal and endometrial cells. The criteria for the diagnosis of carcinoma of the cervix include great variations in size, shape and form of the cells seen in the smear preparation. The most striking variation in shape is seen in the elongated 'tadpole' cells and long fibre-like cells may be seen singly or in groups. Many atypical cells have vacuolated cytoplasm, giving a foamy appearance. The nuclei of the abnormal cells are also varied and bizarre forms occur. Mitoses may be present but are very rare. Histiocytes are often seen in positive smears. Leucocytes are generally present and erythrocytes or evidence of old bleeding are seen in every positive smear. In the diagnosis of endometrial cancer the same general criteria may be applied. The authors conclude from histological evidence that the abnormal cells seen in the vaginal smears were actual tumour cells and did not represent a secondary tissue reaction. In their series of patients 2 with proved cancer had negative smears and therefore in clinically suspicious cases one negative smear is not sufficient evidence to exclude the presence of cancer. It is concluded that this method of examination has proved to be of significant value in the early diagnosis of uterine cancer but an expert knowledge of cytology is necessary. Operation for uterine cancer should not be advised solely from the evidence of a positive vaginal smear, which should be confirmed by biopsy or curettage.

Carcinoma of cervix uteri

Total hysterectomy versus irradiation in early cases.—Jones and Jones compare 36 cases of early cervical carcinoma which were treated by panhysterectomy with 704 cases which were treated with radium alone or with radium combined with X-rays. The 704 cases comprised adenocarcinoma 26, spinal-cell carcinoma 46, transitional-cell carcinoma 543 and 89 cases of spindle-cell carcinoma. The percentage of cure is given for each of the 4 stages of the League of Nations classification but stage (I) only is comparable with the cases submitted to panhysterectomy. It is emphasized that stage (I) includes conditions more advanced than those of patients in the surgical cases whose average of malignant ulceration was 1 centimetre. Survival of over 5 years provided the criterion of cure. The percentage of cure by irradiation was 57.5 and 41.6 was the percentage obtained by panhysterectomy. Of the 36 patients surgically treated 15 survived without recurrence, 2 survived having required radium for recurrence, 15 had died and 4 were untraced. Thirty hysterectomies for transitional-cell carcinoma showed 14 cures. This percentage of 47 compares unfavourably with the 58 per cent cured by irradiation. Too few spindle-cell carcinomas received operative treatment to warrant the making of deductions but surgery could hardly excel the 91 per cent success of irradiation. Two cases of spinal-cell carcinoma received surgical treatment and 6 were irradiated, numbers insufficient to justify deductions. Adenocarcinoma is probably the most favourable form for operation as Martzloff reports 75 per cent of cures, a percentage which contrasts with the 16 per cent cured by irradiation here shown, but again the present surgical series is inconclusive. The 36 hysterectomies included 5 cases of pre-invasive carcinoma; all the patients survived except one who died of post-operative shock. According to the authors, the desirability of operation for early cervical carcinoma is not established and in general irradiation is the treatment of choice.

Carcinoma of corpus uteri

Management and treatment.—Scheffey, Thudium and Farrell publish further observations on

the management and treatment of carcinoma of the fundus of the uterus, based on the study of a series of 127 patients. Of these, 75 were observed for 5 years or more after the diagnosis had been established. Nearly 80 per cent of the women were over 50 years of age, and 78.7 per cent had passed the menopause. In 90 per cent of post-menopausal cases the disease was suspected on account of abnormal bleeding. In the so-called premenopausal cases 7 of the women were over 50 years but suffered from metrorrhagia. The authors point out that in carcinoma of the fundus uteri there is often a long period during which symptoms persist before medical advice is sought. In the premenopausal group the average duration of symptoms was 8 or 9 months, and in the post-menopausal cases from 12 to 13 months. In one patient the disease was discovered because she complained of pain, and in another curettage during a plastic operation showed uterine malignancy. In all gynaecological cases curettage is a valuable diagnostic procedure which should be employed as a routine even if malignancy is not suspected: it may be combined with biopsy of the cervix. In cases of fibromyoma of the uterus in women over 45 years of age an intra-uterine application of radium may be used prophylactically at the time of operation. The indiscriminate use of endocrines for the control of uterine bleeding is condemned even when biopsy precludes malignancy since it is an unnecessarily protracted method of treatment. Among the 127 patients, 114 were suspected of having carcinoma of the fundus; curettage confirmed the diagnosis in 106 cases. Fibromyoma, the most commonly associated lesion, was present in 37.8 per cent of the women; this is in accordance with the observations of other workers. About 11 per cent of the patients suffered from diabetes mellitus. A broad system of classification for cases of carcinoma of the fundus is presented, and for the grading of malignancy the terms 'low grade', 'intermediate grade' and 'high grade' are used, with the rarer adeno-acanthoma separately grouped. Preliminary irradiation with radium combined with a radical operation about 2 months afterwards appeared to be the best procedure and resulted in 5-year cures in 42.9 per cent of patients.

Decker, A., and Cherry, T. H. (1944) *Amer. J. Surg. N.S.*, **64**, 40.

Jones, H. W., Jun., and Jones, Georgeanna E. S. (1943) *J. Amer. med. Ass.*, **122**, 930.

Meigs, J. V., Graham, Ruth M., Fremont-Smith, M., Kapnick, I., and Rawson, R. W. (1943) *Surg. Gynec. Obstet.*, **77**, 449.

Scheffey, L. C., Thudium, W. J., and Farrell, D. M. (1943) *Amer. J. Obstet. Gynec.*, **46**, 786.

VACCINIA AND VACCINATION

See also B.E.M.P., Vol. XII, p. 515; and Cumulative Supplement, Key No. 1595.

Vaccination

Abnormal results of vaccination

Effect on latent tuberculous foci.—Keers and Steen from Tor-na-Dee Sanatorium, Aberdeenshire, report 4 instances of patients in whom vaccination was followed by an immediate flare up of pulmonary tuberculosis. In 2 of these there was not any history of previous symptoms; the other 2 were known cases of tuberculosis in which the disease was quiescent or arrested. The ages varied from 19 to 28 years. A search of the literature revealed 4 similar cases, 2 reported by Blacher in 1931 and 2 by Ainger in 1937. Tuberculous meningitis developed in 3 of these patients. *Per contra*, Stone reported the results of vaccination in 337 tuberculous patients at the Robert Koch Hospital, St. Louis. Only one patient showed any definite pulmonary exacerbation; 2 others had a temporary increase in cough and sputum. The authors consider that special caution should be exercised before known cases of tuberculosis are submitted to vaccination.

Keers, R. Y., and Steen, P. (1943) *Brit. J. Tuberc.*, **37**, 111.

VEIN DISEASES

See also B.E.M.P., Vol. XII, p. 526; and Cumulative Supplement, Key No. 1596.

Varicose veins

Treatment

Hazards attending obliterative treatment.—Atlas mentions severe haemorrhage, inadvertent tying of the femoral vein and injury to the femoral artery as mishaps not unknown in the treatment of varicose veins. The resection of 2 inches of the saphenous vein near its junction with the femoral vein and the subsequent injection of a sclerosing solution into the varicosities was the prevailing method of treatment. The author deprecates the retrograde injection of such a solution at the time of resection since pulmonary embolism and white leg have ensued. Injection into the saphenous system was shown by experiment rapidly to permeate the deep venous tree. Its patency and the rapid blood flow in ambulatory patients which causes speedy dilution of the solution prevents thrombosis which post-operative recumbency encourages. Administration through a ureteral catheter passed down the divided saphenous vein has been practised in order to prevent leakage into the deep venous tree. Again experiment showed that deposition of the solution below the knee failed to prevent leakage into deep veins. Radiography of the veins in the normal subject after diodrast (diodone) had been injected was the

experimental method employed. Ambulatory patients are liable to mishaps local and general. Dangerous reactions may be shown by sensitive individuals especially when quinine-urethane and sodium morrhuate are used. Sensitivity should be tested by the injection of a small initial dose of the intended solution in the varix to be thrombosed. Ulceration arises from extravascular deposition especially of quinine-urethane, the use of which should be discarded, and of hypertonic saline-glucose. Chemical phlebitis is the curative process but if it is employed excessively it may cause prolonged disability. Below the knee the complication most to be dreaded is thrombosis of the popliteal vein. In order to prevent such a complication a tourniquet should be so adjusted as to occlude the lesser saphenous vein before it dips to join the popliteal vein; the tourniquet should remain in place for 5 minutes after the injection has been given.

Atlas, L. N. (1943) *Surg. Gynec. Obstet.*, **77**, 136.

VELDT SORE

See also B.E.M.P., Vol. XII, p. 538.

Clinical picture and complications

Effect of profuse sweating

Review of treatment.—Devine of the Australian Imperial Force records his observations on 200 cases of desert or veldt sore as they occurred in Australian troops besieged in Tobruk in 1941. Idiopathic sores were rare; the majority occurred after a skin injury or infection such as a boil. Profuse sweating contributed largely to the persistence of the lesions, as did the unwillingness of the men to seek treatment until the sores had become indolent and chronic. Stimulating treatment was essential. Sulphanilamide powder showed little effective advantage over eusol (solution of chlorinated lime with boric acid) or cod-liver oil. Chronic cases reacted well to rest in bed and patients who had lost a considerable amount of skin required to have skin grafted on after the surfaces had been rendered healthy by saline baths and sulphanilamide powder. Some of the worst cases may need to be evacuated to cooler areas.

Devine, J. (1943) *Med. J. Aust.*, **2**, 261.

VERTIGO

See also B.E.M.P., Vol. XII, p. 544.

Labyrinthine or aural vertigo

Aural vertigo without suppuration

Ménière's syndrome.—Ménière's disease, Ménière's syndrome or aural vertigo are the names given to a distinct clinical entity. Hallpike describes the vertigo as paroxysmal, often with nausea and vomiting, deafness and tinnitus, but with no other nervous abnormalities. Gross organic changes occurred within the labyrinth and not in the VIII nerve—they corresponded to the state of endolymphatic hypertension postulated by other workers. The histological changes were the same in all cases examined, which suggested that they were due to unilateral disease of the labyrinth. Hallpike gives the results of 2 years' investigation of this disease. A modification of the caloric tests of Bárány was used—2 tests on each ear with water at 30° and at 44° C. Each ear was irrigated for 40 seconds. The resulting nystagmus was measured by the time in seconds which elapsed between the application of the stimulus and the end of the response. The 3 important points in the tests were (1) temperature of the stimuli; (2) intensity of the stimuli and (3) the necessity for the use of both cold and hot stimulation. The principles underlying the tests were as follows. For (1) the external canal was chiefly involved. The deflecting powers of the stimuli upon the cupula should be equal and opposite. The temperatures used were therefore 30° and 44° C., 7° below and 7° above body temperature. For (2) the test should reveal the slightest change in sensitivity of the cupular end organs. For (3) four reactions made up the pattern of a directional preponderance and each ear contributed a particular disturbance of its own to reactions. Two varieties of change in the normal patterns of the caloric responses were found in regard to the direction and the spontaneity or easy evocation of nystagmus; these were attributed respectively to lesions of the utricle and external canal. In 100 cases the author found that 12 gave normal reactions; in 21 there was directional preponderance and in 49 a canal hypofunction. Among other changes encountered, in one case the 2 cold responses were almost equal whereas there was much inequality in the hot responses. This change might be due to lesions of the left canal and utricle in combination.

Histamine treatment of Ménière's syndrome.—The syndrome described by Ménière in 1861 numbers Luther, Swift and probably Beethoven among its illustrious victims. Rainey now describes the effects of treatment with histamine-phosphate. The symptoms which constituted the syndrome are vertigo of terrifying onset, often accompanied by nausea and vomiting, nerve deafness unilateral or bilateral which may be complete or partial, and tinnitus. The suggested causation is oedema of the labyrinth. For administration 1 cubic centimetre of histamine phosphate (2.75 milligrams) is dissolved in 250 cubic centimetres of isotonic sodium chloride solution. During the first 5 minutes of intravenous administration the amount should not exceed 30 drops a minute, as complaint may be made of constriction in the chest. The rate is increased after the first 5 minutes to 70 drops per minute. There is usually

considerable variation in the blood pressure which is taken every 10 minutes. Symptoms to be expected are occipital headache which soon becomes frontal, facial flushing and a transitory erythema of chest and thighs. Two and sometimes 3 intravenous treatments on alternate days are desirable. A subcutaneous maintenance dose, elsewhere advised, is deprecated. Twenty-two patients have been treated since December 1940, women predominating, ranging in age from 40 years to 76. Although 5 failed to respond, in 17 treatment proved successful and they are now well and employed.

Two treatment methods in Ménière's disease.—Cawthorne describes two kinds of treatment in Ménière's disease and reviews other accepted methods. Sedatives have long been used, phenobarbital being the most helpful in preventing spread of the disturbance to the central nervous system as a whole. Histamine is useful in some cases, possibly because allergy is present. Nicotinic acid has been used for its vasodilatation effect. Inflation of the eustachian tube has been practised but is not advocated by Cawthorne. Removal of oronasal sepsis may have improved some cases. For operative treatment, drainage of the saccus endolymphaticus is useful for cases of Ménière's disease with marked deafness on the affected side which does not respond to other treatment; function of the labyrinth is abolished and the procedure is safe. Section of the whole of or of the vestibular division of the VIII nerve has been practised with good results. The disease may cause such distorted hearing that total loss of hearing on the affected side (by severing the cochlear division) is preferred by patients. Injection of alcohol into the perilymphatic space is simple and successful. The author found that combination of hyoscine grain $\frac{1}{100}$, hyoscyamine grain $\frac{1}{150}$, 1 to 3 tablets a day, kept down the attacks. Luminal grain $\frac{1}{2}$ and pilocarpine grain $\frac{1}{10}$, suited some cases better. When conservative measures fail, and when there is much loss of hearing on one side and good hearing on the other, operation is recommended. Cawthorne abolishes labyrinthine function by opening the endolymphatic space. He opens the canal via the mastoid and then uses a Leitz binocular dissecting microscope, magnification 10 diameters. The membranous canal is removed with a fine forceps and the wound closed without drainage. In some cases the exercises devised for the rehabilitation of soldiers suffering from post-concussional vertigo had to be used before the patients were able to return to work.

Cawthorne, T. E. (1943) *J. Laryng.*, **58**, 363.

Hallpike, C. S. (1943) *J. Laryng.*, **58**, 349.

Rainey, J. J. (1943) *J. Amer. med. Ass.*, **122**, 850.

VESICULITIS

See also B.E.M.P., Vol. XII, p. 553.

Acute and chronic

Diagnosis

Importance of differential diagnosis.—Close discusses acute and chronic inflammations of the vesiculæ seminales. Infection ascends from the urethra, as in gonorrhoea, or is haematogenous, as in tuberculosis. Other organisms encountered are the *staphylococci*, *Bacillus coli communis* and the transitory *trichomonas*; the last-named prepares the field for secondary organisms. In acute vesiculitis the pain radiates from the groin and is felt also in the rectum; this pain and the mass felt in examination per rectum are rarely distinguishable from those of prostatitis and differentiation depends upon the wet film. Appendicitis and renal colic require consideration in differential diagnosis. Similar but less acute signs characterize chronic vesiculitis, in which there is occasionally haemospermia. In differential diagnosis it must be remembered that the same kind of groin pain arises from small, but not from large, varicoceles. Gonococcal arthritis, uveitis and fibrosis, especially of plantar type, are incurable in the presence of vesiculitis; hence the significance of its recognition. Abnormal vesicular secretion in the wet film is fibrillar and contains leucocytes and large multiform cells, transparent, granular, without nuclei and often clumped. They may occur in formations which could originate only in ducts of considerable lumen. Their direct aspiration during vasostomy is adduced as a proof that these formations originate in the vesiculæ seminales. When the acute stage yields to the use of sitz baths, alkaline administrations and sulphapyridine, massage is instituted with, later, the passage of sounds and the instillation of increasing strengths of silver nitrate. Progress is estimated by the wet film appearances and the main objective is the patency of the ejaculatory ducts, often heralded by a salutary return of discharge. All persistent non-tuberculous cases are thus treated. In long resistant cases vasostomy has been practised and conclusions are drawn from 57 cases. Thirty-three patients with non-gonococcal urethritis, who had had an average detention in hospital of 50 days before vasostomy, provided satisfactory films 20 days after it. In 24 cases of gonorrhoea with an average pre-operative period in hospital of 60 days patients attained cure 21 days after vasostomy.

Close, W. J. (1944) *Med. J. Aust.*, **1**, 170.

VITAMINS

See also B.E.M.P., Vol. XII, p. 570; and Cumulative Supplement, Key Nos. 1601-1609.

Water-soluble vitamins**Vitamin B₁**

Thiamine metabolism.—The conversion of thiamine chloride (vitamin B₁) into its readily utilizable form of diphosphothiamine (cocarboxylase), and conversely the dephosphorylation of diphosphothiamine, are principally functions of the liver and kidneys. Williams and Bissell investigate the disturbance of thiamine metabolism in hepatic cirrhosis and chronic nephritis; healthy students served as controls. As a preliminary, a specimen of blood for comparison was taken from all subjects, fasting and at rest. In one test the controls ingested orally 15 milligrams of thiamine hydrochloride. Rapid absorption was proved by a raised thiamine blood level 6 minutes later. Speedy phosphorylation to diphosphothiamine, which occurred concomitantly and increased in 15–30 minutes, was also noted. In another test the controls received 15 milligrams of thiamine intravenously with an immediate outstanding rise of the diphosphothiamine blood level, whereas the rise in thiamine level returned to normal in 6 minutes; this is evidence of yet more rapid and extensive phosphorylation. Cirrhotic and nephritic subjects received only the intravenous injection. The relative inhibition of phosphorylation was shown by a smaller rise in the diphosphothiamine level, despite an increased thiamine level. The nephritic subjects showed changes similar to but less rapid than those in the controls. In neither group was the rise in diphosphothiamine proportional to the amount of thiamine injected. The excess of thiamine is probably stored, not excreted. It was however discovered that the administration of mercurphylline increased its excretion. Repetition of intravenous injection with 15 milligrams of cocarboxylase produced in controls a rapid increase of plasma diphosphothiamine and an equally rapid dephosphorylation to thiamine. In cirrhotic subjects the increase of diphosphothiamine was less relatively to the increase of thiamine but its prolonged maintenance above the normal indicated delay in dephosphorylation. The tests on the nephritic subjects gave somewhat similar readings to those on cirrhotic subjects, but whereas the 6-minute diphosphothiamine reading for the cirrhotics was 15 cubic centimetres, that for the nephritics was 80.

Vitamin B₂ complex and the pellagra-preventing (P-P) factor

Ariboflavinosis and the eye.—The relation of the presence or absence in the body of riboflavin (vitamin B₂) to the eye is reviewed by Pirie. Uncomplicated deficiency in man is unknown since other dietary deficiencies are always present. Ocular signs are early noticeable. The patient complains of photophobia and dimness of vision and on examination circumcorneal injection is seen. At a later stage the cornea itself is invaded by vessels and opacities may develop. In animals changes have also been observed in the conjunctiva and in the lacrimal glands. The corneal injection is superficial and symmetrical. Estimation of riboflavin in tissues depends either upon its property of fluorescence or upon its adjuvant influence on the growth of certain bacteria. In the ox's eye it occurs, mainly in the form of the dinucleotide, in the retina and in traces in the vitreous and aqueous, the lens and the substantia propria of the cornea. The Meibomian and lacrimal glands contain more riboflavin compounds than does any other part of the eye.

Fat-soluble vitamins**Vitamin A**

A case of hypervitaminosis A.—Josephs describes a Jewish boy aged 3 years with severe hypervitaminosis A. He had had about 240,000 United States Pharmacopoeia units of vitamin A daily since he was 3 months old. The condition was characterized by hepatomegaly, splenomegaly, hypoplastic anaemia, leucopenia, increased serum vitamin A, increased serum lipoids, advanced skeletal development, clubbing of the fingers and scanty coarse hair. The boy had an abnormal appetite for halibut-liver oil, the source of the vitamin. Most symptoms cleared quickly when the excess vitamin was stopped. Experimental and clinical observations with excess vitamin A and carotene in animals and man indicate the existence of a mechanism for the maintenance of a constant level of vitamin A in the blood—which is possibly related to the activities of the reticulo-endothelial cells—but no such mechanism seems to exist for carotene. The development of hypervitaminosis A in this child indicates either that some defect existed in the system responsible for the protective reaction or that intense prolonged overdosage is capable of injuring the regulating mechanism. The effect on man of ingesting large amounts of carotene has been much studied, but knowledge of excessive dosing with vitamin A has been gained almost entirely from observations on rats and mice. Only artificial concentrates contain enough vitamin A to be dangerous to man. The margin of safety between an adequate prophylactic dose and a dangerous dose is very wide.

Josephs, H. W. (1944) *Amer. J. Dis. Child.*, **67**, 33.

Pirie, A. (1943) *Brit. J. Ophthalm.*, **27**, 291.

Williams, R. H., and Bissell, G. W. (1944) *Arch. intern. Med.*, **73**, 203.

VULVA AND VAGINA DISEASES

See also B.E.M.P., Vo^l. XII, p. 606.

Vulva**Atresia**

Occurrence in young children.—Bowles and Childs consider that atresia of the vulva, unlike

atresia vaginae, is almost always an acquired and not a developmental condition. Of 20 cases tabulated one patient had the condition at birth, 15 acquired it; of 4 information was lacking. It has been stated that the condition is caused by a local irritation as a consequence of acute infective fevers but the authors have failed to find a report of an authenticated case. Whether the postulated raw surface arises from friction of the diaper or from too vigorous scrubbing remains unknown. Fourteen infants in the authors' series were under one year of age and of the remainder the oldest was aged 5 years. Examination of the genitalia at birth and subsequently by the practitioner is desirable, as well as constant inspection by the mother who should exercise gentleness in cleansing. Usually, firm separation with the infant in the lithotomy position suffices, without anaesthesia. Having ensured dryness of the patient's skin, the operator, wearing dry rubber gloves, can readily exert sufficient traction. Blunt dissection with probe or haemostat may be required in order to free the lowermost portion of the fused area which, being denser, is probably formed first. Thenceforward the fusion is usually continuous to the opening maintained by the passage of urine. Vigilance and the application of boracic acid to the raw surfaces will prevent re-coalescence. When the union is firmer and the patient is older the administration of anaesthesia is necessary, because sharper dissection and occasionally the suturing of raw edges has to be carried out. Vomiting and nocturnal crying occurred in one patient, dysuria in a second and enuresis in a third; in the other patients symptoms were absent. Persistence of the adhesion causes infection of the urinary tract and the case is appended of a woman aged 74 years in whom such fusion led to incontinence, failing vision, abdominal pain and inability to walk.

Vagina

Vaginal fistulae

Management of urogenital fistula.—The management of some of the more difficult forms of urogenital fistula occurring in women is described in considerable detail by Cooke. Operation should be undertaken only when inflammatory processes have been reduced to the minimum and when natural repair is at a standstill. Fine chromized catgut is recommended for sutures and buried knots should be avoided. Post-operative bladder drainage is important in order to reduce risk of suture breakages which are most likely to occur in from 5 to 8 days after operation. Whenever possible suture of the vesical mucosa should be avoided. In fistula involving one-third of the urethra and with too extensive a defect and too much scarring of the bladder wall to allow approximation, the defect must be closed with a tissue flap covered with epithelium derived from the vaginal wall and carefully cut to the proper dimensions. A fistula which involves the posterior wall of the bladder above the interureteral ridge may be too large and there may be too much scar tissue to allow the bladder defect to be remedied. In such cases mobilization of the postero-superior wall of the bladder by the suprapubic trans-vesical approach is difficult and dangerous. By an alternative procedure the wall of the bladder above the fistula is sutured to the cervix and the lower edge of the fistula is closed by suture to the reflected margin of the cervico-vaginal mucosa. Another type of fistula occurs above the anterior cervico-vaginal reflection as a result of anterior laceration of the cervix from forcible delivery through the partially dilated cervix or from rapid dilatation in cases of senile cervix. This type is closed by mobilization of the bladder wall up to the uretero-vesical fold of peritoneum and of the posterior wall of the bladder, with closure of the fistula in the bladder and closure of the cervical tear. The anterior vaginal wall is then sutured to the cervix at as high a point as possible. In cases of vesico-uterine fistula occurring after anterior laceration of the cervix the operation may be difficult owing to the dense scar tissue and care must be taken to avoid perforation of the vesico-vaginal fold of peritoneum. A large transverse vesico-vaginal fistula with destruction of the inner portion of the transvesical ureter may occur after total hysterectomy. It is difficult to establish an adequate ureteral ostium but subsequent stenosis of the ostium is prevented by cystoscopic dilatation. In uretero-vaginal fistula occurring after hysterectomy it is exceedingly difficult to find and to dispose of the ureter and also to effect a uretero-ureteral anastomosis after resection of part of the ureter: it is generally necessary to implant the ureter into the bladder. Simple closure of the fistula in almost all such cases is useless; an alternative repair procedure is described.

Bowles, H. E., and Childs, L. S. (1943) *Amer. J. Dis. Child.*, **66**, 258.

Cooke, W. R. (1943) *Urol. cutan. Rev.*, **47**, 609.

WHOOPIING-COUGH

See also B.E.M.P., Vol. XII, p. 616; and Cumulative Supplement, Key No. 1613.

Diagnosis and differential diagnosis

Examination of a swab

Use of penicillin.—Haematological examination in cases of early pertussis shows leucocytosis with relative and absolute lymphocytosis, and plates of Bordet-Gengou medium on which the child has coughed often yield the organism but according to Cruickshank a method comparable to that of the diphtheria swab would be a boon to the practitioner. The method proposed is founded on the resistance of *Haemophilus pertussis* to penicillin. Of 52 swabs positive on the penicillin plate 5 only were positive on the plain plate. The strength of penicillin

inhibiting the growth of test organisms is from 15 to 25 Oxford units for each plate of 12 cubic centimetres of Bordet-Gengou medium. From 4 to 8 drops of the penicillin are spread-over the plate half an hour before the latter is to be inoculated and the plate is dried in the incubator. In 250 cases diagnosed as pertussis a metal throat swab bent half an inch from the end was rubbed on the post-nasal pharyngeal wall in order to obtain material for the inoculation of the penicillin plate. At the same sitting a cough plate, without penicillin, was exposed to a paroxysm. On examination by hand lens after 3 days' incubation, colonies removed and emulsified in saline solution were tested by slide-agglutination with high titre serum. After allowing for certain failures and diagnostic errors 50 per cent of patients were adjudged to be past the infectious stage. Of 90 positive cultures attained, 40 were given by both penicillin and cough plates, 23 by cough plate only and 27 by penicillin plate only, the penicillin plate having an advantage of 4.4 per cent, with more luxuriant growth. Improved swab taking would improve results and since the swab, resting on solid saline agar, remains vital for 24 hours the evolution of a postal service seems to be possible.

Treatment

Preventive

Prophylactic doses.—McGuinness, Armstrong and Felton report on hyperimmune human serum in the prophylaxis and treatment of pertussis and describe the serum which is now employed. Donors receive a total of 7 cubic centimetres of vaccine which contains 15,000 million organisms per cubic centimetre, in 4 weekly injections. They receive 0.5 cubic centimetre in each arm on the first occasion and 1 cubic centimetre thereafter. A month later their serums are titrated and donors whose titre exceeds 1 in 2,560 are selected. At each monthly bleeding titration is repeated and a further 2 cubic centimetres of vaccine is administered in order to maintain the titre. The essential prophylactic dosage for children irrespective of age is 2 injections of 20 cubic centimetres each, preferably into the buttock. A first injection within 48 hours of exposure is followed by a second 5 days later, but 3 days is the appropriate interval if initial injection is delayed. Of 308 cases so treated of exposure which was either intimate and continuous or intimate but brief, 186 escaped infection, 44 were affected mildly (without vomiting) or very mildly (neither whooping nor vomiting) and 19 displayed typical pertussis. Of 59 patients who were only casually exposed 56 escaped, 2 were mildly or very mildly affected and one displayed typical pertussis. In the treatment of established whooping-cough not less than 3 injections of 20 cubic centimetres of serum at 48 hours' interval are required, regardless of age. Relapse 5–7 days later may necessitate a fourth dose. Serious illness, especially broncho-pneumonia, may require several doses of 50–100 cubic centimetres given intravenously. The response by 436 patients is classified as excellent or good in 310, moderate in 88 and poor in 38. In addition 6 fatalities occurred, but none of the patients had received the dosage now considered to be adequate. Five were children under 6 months old. Otherwise there did not appear to be any direct relation between age and rate of recovery. There were 55 children under the age of 2 years who were known to have had broncho-pneumonia before serum therapy was instituted, of whom 10 received sulphathiazole or sulphadiazine; in 8 the result of the combined treatment was excellent or good and the other 2 were classified as moderate and poor respectively. The administration of toxoid or purified agglutininogen to donors is being undertaken experimentally.

Use of antitoxic serum

Ospeck and Roberts have made experiments which show that the active and passive protection of mice and rabbits against large doses of pertussis toxin or live culture is due to the antitoxin content of the pertussis serum. A passive protection test has been developed which shows the difference in protection produced by the injection of antitoxic and of antibacterial serum in mice; the experimental dose of live culture is given intracerebrally and that of toxin intravenously. The intraperitoneal technique shows this difference too but only small doses can be given. In the intracerebral technique the challenging dose of live culture or of toxin could be much larger if there were a strong enough protective serum. The authors used 25 minimum lethal doses of toxin and 60 of live culture with their serum, which contained 15,000 units per cubic centimetre and protected against the toxin and live culture doses in a 1 in 5 dilution. Antibacterial serum or weak antitoxic serum showed no protection at all under the same conditions at 1 in 5, or in undiluted strengths. The authors' test was economical in materials. Thus 60 minimal lethal doses of live culture given intracerebrally represented 300 million organisms, whereas 10 minimal lethal doses given intraperitoneally represented 20 billion organisms. These features led to an increased sensitivity of their test. The authors used 0.2 cubic centimetre of serum intramuscularly. The intracerebral test did not give satisfactory results with small experimental doses of live culture. Since protection against live culture or toxin is due to the antitoxin in the serum, it is best to use the toxin-antitoxin neutralization test for testing weak serum. A challenging dose of toxin gives a clearer endpoint than does that of live culture, especially in low titre serum. Normal mice injected intracerebrally with live culture or with toxin showed the same series of symptoms before death; within 96 and 48 hours respectively paralysis was complete; the symptoms were due probably only to the toxin. The mice usually died about 36 hours later. These symptoms could be prevented by previous injection of antitoxin but not of antibacterial serum. The antitoxic serum which gave most protection in these passive experiments was obtained from rabbits

which had been given a long series of toxoid injections. Normal rabbits can be passively protected for about 18 days by the injection of antitoxic serum.

Cruikshank, R. (1944) *Lancet*, **1**, 176.

McGuinness, A. C., Armstrong, Janet G., and Felton, Harriet M. (1944) *J. Pediatr.*, **24**, 249.

Ospeck, Anne G., and Roberts, M. E. (1944) *J. infect. Dis.*, **74**, 22.

YAWS

See also B.E.M.P., Vol. XII, p. 631.

Clinical picture

Tertiary stage: tertiary lesions of skin and bone

Radiographical appearances of lesions.—Goldmann and Smith report on the radiological appearances of bones in yaws in the tertiary stage from a station in Sierra Leone, where yaws is practically endemic and syphilis is common. The great majority of enlisted native soldiers show evidence of a previous infection by yaws; there may be scars, velvet-like, slightly depressed, often pigmented and scattered over the trunk and extremities; localization of the lesions on the legs is very common and the tibiae often show the 'boomerang' deformity described in 1936 by Hackett in Australian aborigines. Goldmann and Smith's observations were based on 185 radiological examinations from which 101 were selected for this report. Radiology provided a means of differentiating the stages of yaws lesions. The tibiae were most often affected and the fibulae came next. The vertebrae were involved in about 5 per cent of the authors' cases; the vertebral bodies when affected were eburnated (marbled), with a zone of osteosclerosis.

Goldmann, C. H., and Smith, S. J. (1943) *Brit. J. Radiol.*, **16**, 234.

YELLOW FEVER

See also B.E.M.P., Vol. XII, p. 660; Interim Supplement, No. 17*; and Cumulative Supplement, Key No. 1616.

Types and their geographical distribution

Outbreak in the Nuba Mountains

Methods of control.—Kirk publishes observations on the study and control of yellow fever in Africa, with particular reference to the Anglo-Egyptian Sudan. He states that the nature of the infection in Africa is essentially rural, although most of the epidemics hitherto recorded have been of the urban type. The immunity survey initiated 10 years ago showed that many of the population were immune to yellow fever in a broad band of territory extending from the West Coast eastward as far as the Nile, although clinical cases had been seen only in the western part of the area. An obscure jaundice which occurs in the Sudan has been shown not to be due to yellow fever. In 1940, however, an extensive epidemic of rural yellow fever occurred in the Nuba Mountains district of the Sudan. Several different vectors appeared to be concerned in the transmission; *Aedes aegypti* was probably of little or no importance since the density of this mosquito in the region was not above that generally considered sufficiently low to prevent epidemic spread. Measures designed to limit the spread of the disease included the establishment of a sanitary cordon around the whole Nuba Mountains district. All movement into or out of the area by road, river, rail or air was prohibited, except that a quarantine was established at one point to allow the entrance and exit of essential staff and supplies. The period of quarantine was 10 days. Supplementary measures to control movement were taken outside the affected area. Vaccination was practised on a large scale. With the seasonal drying up of the country mosquitoes largely disappeared. The epidemic came to an end without the occurrence of any known case outside the originally affected area. It was impossible to estimate whether or not the measures instituted were responsible for checking the spread of infection.

Kirk, R. (1943) *Trans. R. Soc. trop. Med. Hyg.*, **37**, 125.

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